

LECTURE NOTES OF INTERNAL MEDICINE

- Nutrition
- Therapeutics
- Infections & Tropical Diseases

- Immunology
- Genetics
- Toxicology
- Geriatric Medicine
- Metabolic Diseases

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NUTRITION

Classification of nutritional disorders:

Undernutrition: Insufficient food energy causing starvation in (adults), Marasmus in (children).

Malnutrition: Deficiency of protein or other essential nutrients.

Obesity: Positive energy balance.

Nutrient excess: Iron overload, vitamin D excess.

Effect of toxicants in food:

e.g. coeliac disease, urticaria, favism and migraine.

Subdivision of nutrients:

- Water.
- Macronutrients e.g. carbohydrates, fats, protein and dietary fibres.
- Organic micronutrients (vitamins).
- Inorganic micronutrients (electrolytes, minerals, trace elements).

Adult requirements for nutrients

g/d	
1 Kg (1 L)	Water.
50-100 gm	Carbohydrates.
50 gm	Proteins.
1-5 gm	Na, K, Cl, essential fatty acids.
1 gm	Ca, P.
mg/d	
50 mg	Vitamin C.
15 mg	Niacin, Vitamin E.
1-2 mg	Vitamin A, Thiamine, B ₂ , B ₆ .
µg/d	
200 µg	Folic acid.
2-10 µg	Vitamin B ₁₂ , D and K.



Different Food Stuffs

I. Carbohydrate (CHO): they provide major part of the energy (4 Kcal/gm).

Available sugars

Monosaccharides (glucose, fructose).

Disaccharides (sucrose, lactose, maltose).

Available polysaccharides

(Starch, Glycogen).

Unavailable polysaccharides

(Most of dietary fibers).

Dietary fibres:

They are plant foods which do not digested by human enzymes e.g. cellulose, hemicellulose, lignins, pectins and gums.

Value:

- TTT of obesity.
- TTT of Dumping \$.
- TTT of irritable bowel disease.
- TTT of Constipation.
- TTT of diverticulosis.
- TTT of DM.

Gylcemic index

- It quantifies the effect of different CHO on the blood glucose.
- It is high for bread, potatoes and glucose.
- It is low for pasta, legumes and grain cereals.
- The index may be useful in constructing therapeutic diet for diabetes.

II. Fats: They give high caloric value (9 Kcal/gm).

- Saturated fats e.g. palmitic and stearic → ↑ LDL, ↑ cholesterol.
- Polyunsaturated fatty acids e.g. arachidonic and linoleic.

The principal polyunsaturated fatty acid in plant seed oils is linoleic (they are good for coronary heart disease).

III. Proteins

These are made up of some 20 different amino acids, of which nine are essential for normal synthesis of different proteins in the body, these essential or indispensable amino acids are:

- | | |
|------------------------------|---------------|
| • Phenyl alanine + tyrosine. | • Valine. |
| • Tryptophan. | • Isoleucine. |
| • Histidine. | • Leucine. |
| • Methionine + cysteine. | • Lysine. |
| • Threonine. | |

NB:

- The dispensable amino acids can be synthesized in the body by transamination provided that there is sufficient supply of amino groups.
- Proteins of animal origin e.g. eggs, milk, are generally of higher value than proteins of vegetable origin which are deficient in one or more of the essential amino acids.



Daily energy requirements/d

- Male office workers in industrial countries needs 2500 Kcal.
- Male farmer needs 3000 Kcal.
- Male doing heavy work needs 3500 Kcal.
- House wife in industrial countries needs 2000 Kcal.
- Women in developing countries needs 2250 Kcal.

Cause of undernutrition in adults

- Insufficient food.
- Anorexia.
- Malabsorption.
- Persistent regurgitation or vomiting.
- Increased BMR e.g. thyrotoxicosis, infections.
- Loss of calories in urine e.g. glycosuria in DM.
- Cachexia in some cases of cancer.

Some Important Elements

Phosphorus

It is used by the body in the form of phosphates, which are present in many biochemical compounds.

Causes of hypophosphatemia

- Renal tubular phosphate loss.
- Prolonged intake of aluminium hydroxide antacids.
- TPN (see later).
- Alcoholism.

NB: Hypophosphatemia → ↓ ATP → muscle weakness.

Cause of hyperphosphatemia

- Hypoparathyroidism.
- Acromegally.
- Renal failure.

Iodine

- It is present in sea foods.
- Its deficiency leads to endemic goiter.
- Endemic goiter nowadays is decreasing due to use of iodised salts.



Fluoride

- It presents in teeth, preventing dental caries.
- The chief source is drinking water, sea-fish and tea.

Fluorosis (When the water fluoride is high)

There is mottling of the teeth + loss of lustre of the enamel.

Chronic fluoride poisoning (industrial)

The skeleton shows increased density of bone in spine, pelvis, and limbs with calcification of ligaments and tendinous insertions of muscles.

Zinc

Zinc is an essential component of many enzymes including carbonic anhydrase, alcohol dehydrogenase, alkaline phosphatase, lactic dehydrogenase, superoxide dismutase and pancreatic carboxypeptidases. Also it helps RNA & DNA stabilization.

Causes of Zinc deficiency

- Intestinal disorders.
- Hemodialysis.
- Chronic alcoholism.
- Burns.
- Anorexia nervosa.
- Nephrotic syndrome.
- DM.
- Chronic febrile illness.
- TPN without zinc.

Sources of Zinc

- Wheat.
- Liver, beef.
- Sardines.
- Cereals.

Acute zinc deficiency

- Diarrhea, mental apathy.
- Dermatitis.
- Loss of hairs.

Chronic deficiency

- Dwarfism.
- Hypogonadism.

Selenium

It is a part of the enzyme glutathione peroxidase which helps to prevent hydroperoxidase from accumulation in lipids of cell membranes (it is a natural antioxidant).

Another function, it is a part of enzyme responsible for conversion of thyroxine to tri-iodothyronine in liver microsomes.

Ca and Mg	→	see Endocrine
Na and K	→	see Electrolyte imbalance
Iron	→	see Blood
Copper	→	see Liver

Copper deficiency: This leads to anemia, retarded growth and skeletal rarefaction.

Chromium: It facilitates action of insulin so its deficiency leading to → hyperglycemia.

Therapeutic Diets or Diet Therapy

Clear Liquid Diet

This diet provides adequate water up to 1000 kcal as simple sugar and some electrolytes.

Uses of this diet:

- (1) Postoperative status.
- (2) Upper gastrointestinal lesions.
- (3) Difficulty in swallowing

Full Liquid Diet:

This diet provides adequate water, sugar, dairy foods, soups, eggs and strained fruit juices. It is used in difficulty in swallowing or chewing. This diet can be used following clear liquid diet.

Low-residue diet:

- It contains easily assimilable proteins and carbohydrates.
- It includes eggs, cheese, fish, chicken cereals, cakes. It is used for ulcerative colitis.

Soft (bland) diet:

It involves minimal chewing: e.g. fish, eggs, cheese, cream, potatoes. It is used for gastrointestinal disturbances e.g. peptic ulcer.

Low fat diet (50 gm/d):

Reduction of fat (10-25 % less than usual intake) may be useful in controlling fatty acid diarrhea. Also low saturated fat diet is required for coronary heart disease and hyperlipidemia.

Low protein diet (50gm/daily):

It is used in renal failure or LCF (hepatic encephalopathy) and with inborn errors of amino acid metabolism.

Low CHO, high protein, high fat diets:

It is used in TTT of hypoglycemic states e.g. (postprandial hypoglycemia).

High-Calcium diets:

For prevention of post-menopausal osteoporosis, 1 gm of Ca/d & 1.5 gm/d for postmenopausal women

Low gluten diet:

This diet eliminates gluten containing food such as wheat, oats, rye... It is used in gluten induced enteropathy.

Dietary fiber:

Diets provide fiber e.g. fresh fruits, fresh vegetables. It is used in constipation, diverticulitis, I.B.D. and D.M as it decrease absorption of CHO. It also reduce cholesterol levels.

Q Non-pharmacological treatment of hypertension

- Reduce sodium intake.
- Increase potassium intake.
- Restrict alcohol.
- Weight reduction.

Q Food allergy and intolerance !? (see immunology).



Tube (enteral) Feeding

There are three general types:

- (1) Blended, strained preparations made from common foods.
 - (2) Those with a milk base to which other foods may be added.
 - (3) Commercial preparations, (expensive)
- Tube feedings are employed when the patient is unable to take food by mouth.
 - Feeding may be administered through a pliable polyethylene nasogastric tube.

Indications:

1. Oesophageal dysmotility or obstruction.
2. Unconsciousness.
3. Neurological in-coordination of swallowing: e.g. stroke.
4. Postoperative.
5. Inflammatory bowel disease.

Caution:

- (1) Dilute material, administer slowly.
- (2) Rate is usually 3L/24 hours.
- (3) Warm fluids to body temperature.
- (4) If diarrhea occurs add 15 ml of pectin.
- (5) Prevent dehydration, hyperosmolality and azotemia by providing adequate water to allow for the solute load and permit normal excretion.

Advantage:

- (1) Fluid and electrolyte imbalance are rare.
- (2) Safe, easy.
- (3) We can provide all food stuffs.

Complications

- Diarrhea.
- Aspiration.
- Oesophagitis.
- Mild metabolic disturbances.

Total Parenteral Nutrition (TPN)

This is called intravenous hyperalimentation. When it is not possible to provide adequate nourishment by the normal alimentary route, all required nutrient substrates may be administered totally by parenteral means.

Indications of TPN

- (1) Chronic inflammatory bowel diseases.
- (2) Prolonged ileus.
- (3) Acute renal failure.
- (4) Acute pancreatitis.



Types:

1- TPN through central venous catheter:

The large vein diameter is necessary to administer the high osmolality solutions of concentrated dextrose and amino-acids without causing sclerosis of the vein, for this reason the TNP solution should not be given through a peripheral vein. So we insert a subclavian vein catheter.

2- Peripheral alimentation:

Because TPN through central vein carries with it a significant number of complications, the peripheral alimentation has increased in popularity, we use solutions with low osmolality. Heparin, steroids and nitrates patches can be used to reduce the occurrence of thrombophlebitis. It can be combined with oral or tube feeding.

Complications

(1) Metabolic complications:

- | | |
|--------------------------------|---------------------|
| - Hyperglycemia. | - Hypoglycemia. |
| - Hyperkalemia. | - Hypokalemia. |
| - Hypercalcemia, Hypocalcemia. | - Reactions to A.A. |

(2) Infections:

(3) Catheter complications, e.g. embolism, pneumothorax and thrombosis.

Methods

The total parenteral nutrition solutions must provide sufficient calories, proteins, vitamins and minerals to maintain basal metabolism and promote growth and tissue healing.

Examples of TPN regimens:

I- Central: (the total fluids infused over 24 hours)

- Amino-acids 14 gm/L (one litre).
- Glucose 50% (0.5 litre).
- Glucose 20% (0.5 litre).
- Lipids 10% (0.5 litre).

II- Peripheral: (the total fluids infused over 24 hours)

- Amino-acids 9 gm/L (one litre).
- Glucose 20% (one litre).
- Lipids 20% (0.5 litre).

N.B.:

- Fat infusions are not hypertonic.
- We can give electrolytes, vitamins and trace elements with the above regimens.
- The basic solutions must be modified to meet specific individual requirements, especially for patients with **D.M. hepatic failure, renal failure and electrolyte disorders.**



VITAMINS

Hypervitaminosis states

Hypervitaminosis A

- This disorder is rare in adults, but it may occur as a result of chronic excessive ingestion of vitamin A.

C/P:

- Anorexia -loss of weight - dry and fissured skin - brittle nails.
- Hypercalcemia, chronic high doses may lead to liver damage, pseudotumor cerebri (benign increase of I.C.T).

Investigations: High serum level of vitamin A.

TTT: Withdraw the medicinal source.

Hypervitaminosis D

This disorder is usually caused by excessive intake of the vitamin.

C/P: Manifestation of hypercalcemia which may progress to renal damage and metastatic calcification.

Investigation: High serum Ca (normal level 8.5-10.5 mg/dl).

TTT:

- Withdrawal of the medicinal source.
- TTT of hypercalcemia (see endocrine).

Hypervitaminosis K

Large doses of water soluble vitamin K to infants, particularly premature infants, may cause hemolytic anemia, hyperbilirubinemia and hepatomegally.

Vitamin A (Retinol)

Sources

- Provitamin A (carotenes) in pigmented vegetables and fruits e.g. Carrots, dark green leafy vegetables and apricots.
- Preformed vitamin A in animal origin e.g. liver and milk.

Functions

- Integrity of epithelial cells.
- It is an essential component for the retinal pigment (rhodopsin) for dim light vision.
- It is called the anti-infective vitamin.



Vitamin A deficiency

1- Epithelium changes:

- The skin will be characteristically dry, scaly and rough (follicular hyperkeratosis).
- Keratinising metaplasia of the epithelium of nose, nasal sinuses, pharynx & tracheobronchial tree with increase liability to infections in these tissues.
- Bitot's spots which are white plaques, triangular formed from desquamated thickened conjunctival epithelium.

2- Eye changes

- Night blindness, xerophthalmia, keratomalacia and blindness.

3- Recurrent respiratory infections and gastroenteritis especially in children.

TTT of vitamin A deficiency

- Single oral dose of retinol 60 mg or by I.M. injection. It can be repeated during follow up.

NB: Carotenes (pro-vit A) has antioxidants effect and give protection against cancers.

Vitamin D

SOURCES: Egg, liver, fish, cod liver oil.

- The natural form, cholecalciferol is formed in the skin by the action of ultraviolet light on 7-dehydrocholesterol.
- Cholecalciferol is hydroxylated in liver cells to form 25-hydroxy-cholecalciferol.
- In kidneys further hydroxylation will produce 1,25-dihydroxycholecalciferol which is the metabolically active form of the vitamin.

Vitamin D deficiency:

This results in:

(A) Rickets

- This occurs in children.
- There will be deficiency of bone mineralization with bone deformities. These deformities include: enlargement of osteochondral junctions (rachitic rosary), bow legs, narrowing of pelvis (contracted pelvis).
- Serum changes include:
 1. Serum calcium usually falls with prolonged vitamin D deficiency.
 2. Decreased serum phosphorous.
 3. Increased serum alkaline phosphatase.

(B) Osteomalacia: → See rheumatology

- This occurs in adults especially during pregnancy and lactation due to the increased demand for vitamin D.
- There will be defective mineralization with development of bone cysts and softness of bones.

Alphacalcidol (one alpha), 1- α -hydroxycholecalciferol, is a synthetic analogue which is converted into 1,25(OH)₂D in the liver without the need for hydroxylation in the kidney. It is used in treating hypocalcemia and osteomalacia due to renal disorder e.g. (chronic renal failure).



Vitamin K (The Koagulation Vitamin)

Sources:

- Vit. K₁ (phytomenadione) is present in green leafy vegetables e.g. spinach, cabbages, peas and cereals, tomatoes, egg yolk, and liver.
- Vit. K₂ (menaquinone) synthesized by bacteria flora in the large intestine.

Summary for Vit K functions:

- Essential for prothrombin (factor II) & also essential for synthesis of other plasma clotting factors (VII, IX and X).
- It is required for synthesis of an amino acid (**carboxyglutamic**), which is part of the protein molecule of the mentioned four coagulation factors.

Vitamin K has important roles in these situations

1. In newborn, primary deficiency can occur because placental transfer of vitamin K is inefficient, the neonatal bowel has not yet acquired bacteria and breast milk contains little amount of the vitamin. Vitamin K is given routinely to newborn babies to prevent hemorrhagic disease of the newborn.
2. In obstructive jaundice, dietary vitamin K is not absorbed and it is very important to administer the vitamin before biliary surgery.
3. Oral anticoagulants act by antagonizing vitamin K.

Vitamin C

- Ascorbic acid is a modified simple sugar.
- It is the most active reducing agent in living tissues.
- Its high concentrations are in the pituitary and adrenals, the eye and white blood cells. It is very easily destroyed by heat, alkalies such as sodium bicarbonates.
- No evidence that it will prevent common cold?!

Dietary sources of vit C

- Guavas, cauliflower.
- Potatoes, cabbage.
- Citrus fruits, green peppers.
- Liver is the only animal source.

Deficiency of vitamin C:

This will result in a disease termed Scurvy (it was discovered when occurred in men with Vasco da Gama due to consumption of diet devoid of fresh fruits and vegetables for long time).

This disease is characterized by:

- 1- Looseness of teeth, inflammation of gums (gingivitis) and bleeding from gums.
- 2- Delayed healing of wounds and easy fracturability of bones.
- 3- Multiple S.C. haemorrhages and increased liability for infections.
- 4- Iron deficiency anemia (vit c keeps iron in ferrous state).

TTT of vit C deficiency

- The normal adult body contains about 1.5 gm of vit C, so 250 mg TDS orally will saturate the tissues quickly.



A.B.: Scurvy appears in man after 3-5 months of ascorbic acid deficiency due to slow metabolism of pre-existed vitamin C in body. Its deficiency results in defective formation of collagen due to failure of hydroxylation of proline to hydroxyproline, the characteristic amino acids of collagen.

A.B.: Very large doses of vitamin C can lead to gastric irritation, diarrhea and oxalate stones as it is metabolized to oxalate.

Vitamin B1 (Thiamin)

Dietary source → Wheat, Nuts, Oatmeal, White bread, legumes and yeast.

Deficiency

- **This results in a disease called beri-beri** (the word comes from Sinhalese language and means "I Cannot" said twice signifying that the patient is too ill to do anything).
- The major manifestations of beri-beri are produced from accumulation of pyruvic and lactic acid (peripheral vasodilatation → hyperdynamic circulation) in blood as a result of failure to form TPP (thiamine pyrophosphate) which is a coenzyme for the decarboxylation of pyruvate to acetyl coenzyme A. this is the bridge between anaerobic glycolysis and krebs cycle.
- So, the cells can't metabolise glucose aerobically, this is likely to affect the nervous system first, since it depends entirely on glucose.

NB: High CHO diets, heavy alcohol intake or intravenous glucose infusions predispose to and aggravate thiamine deficiency.

Manifestations of thiamine deficiency:

A- Beri-beri is characterized by peculiar changes in peripheral nervous system, GIT and CVS including:

- 1- Peripheral polyneuritis with numbness, tender calf muscles and muscle wasting (dry beri-beri).
- 2- Edema (due to toxic effect of accumulated pyruvic and lactic acid on the capillary wall → vasodilatation)
- 3- Palpitation and high cardiac output heart failure.
- 4- Gastrointestinal disturbances e.g.: anorexia, nausea & vomiting.

B- Wernicke's encephalopathy (it presents acutely)

Confusion, ophthalmoplegia and ataxia, these respond to thiamin, but a memory disorders (korsakoff's psychosis) may persist which characterized by impaired memory + confabulations.

Diagnosis of beri-beri

- Measurement of transketolase activity in red cells (TPP is a coenzyme for transketolase).
- Plasma pyruvate and lactic acids are elevated in acute forms of thiamin deficiency.



TTT of beri-beri

- 50 mg thiamin IM for 3 days then 10 mg 3 time/d oral until convalescence is established.

TTT of Wernicke's encephalopathy

- It should be treated without delay by 50 mg thiamine I.V. followed by 50 mg I.M. daily for a week.

Vitamin B2 (Riboflavin)

Dietary source: Liver, Milk, Cheese, Mushrooms.

Deficiency

This results in non-specific manifestations that include:

- 1- Stomatitis and fissures at angles of mouth (angular stomatitis)
- 2- Superficial vascularization of the cornea
- 3- Seborrheic dermatitis (see dermatology) of the face.
- 4- Glossitis.
- 5- Cheilosis; Zone of red, denuded epithelium at the line of closure of the lips, it often associated with angular stomatitis.

TTT: Riboflavin 5 mg TDS orally.

Niacin (Nicotinic acid)

It is called pellagra preventive factor (p.p. factor)

Sources and absorption:

- Sources: liver, kidney, fish, meat, peanuts, yeast and coffee.
- Additional source is by synthesis from the amino acid tryptophan in body (60 mg tryptophan can give rise to 1 mg nicotinic acid).

Requirements: 20 mg/ day.

Deficiency

Results in a disease called pellagra which is characterized by:

1 - Skin: (erythema resembling severe sunburn)

- Which affects skin exposed to sunlight and subjected to pressure, heat and other types of trauma or irritation e.g. face, neck, dorsal surfaces of the wrist and forearms. Also the skin over the greater trochanter can be affected.
- The skin is erythematous, later it becomes brown, thickened, rough and scaly.



2 – Alimentary tract:

- Diarrhea and other gastrointestinal disturbances e.g. anorexia, nausea, vomiting, abdominal pain, achlorhydria (40% of cases), stomatitis with reddening of the tip and margin of tongue (glossitis).

3 – Nervous system:

- Delirium in the acute form of disease and dementia in the chronic form of disease.
- Other neurological manifestations → (see neurology).

TTT → Nicotinamide 100 mg/6 hrs orally.

Pellagra occurs in maize eating population due to:

- Maize is deficient in nicotinic acid.
- Maize is deficient in tryptophan (from which nicotinic acid can be synthesized).
- Maize contains nicotinic acid antagonists

It is diagnosed by assay of RBCs NAD.

Pyridoxine = Vitamin B6

SOURCES: liver, cereals, peanuts and bananas.

Requirements: 2 mg / day.

Functions: The active form of the vitamin in man is pyridoxal 5 phosphate which is an important coenzyme involved in many metabolic reactions in amino acids metabolism including aminotransferases.

- Some cases of sideroblastic anemia respond to TTT by pyridoxine

Deficiency

1. Epileptiform convulsions in infants, neuropathy.
2. Hyperirritability and gastrointestinal distress.
3. Anemia, leucopenia, failure to maintain growth in animals.
4. Vitamin B₆ decreased in females under pills causing depression, this can be treated by by vitamin B₆

NB: INH and penicillamine act as chemical antagonists to pyridoxine

Folic Acid

= Folic acid = pteroylglutamic acid → See Hematology

Vitamin B12

= Cyanocobolamin = anti-pernicious anemia → See Hematology

Therapeutics

Antibiotics

Penicillins (beta-Lactam)

Mechanism

- Bactericidal via inhibiting the synthesis of bacterial cell wall.
- They are active against both gm +ve and certain gm -ve organisms.

Classification

1. Broad spectrum penicillins: (semisynthetic) (their spectrum includes gm -ve bacteria)

- **Ampicillin:** with dose of 0.25-1 gm/6 hours (It causes diarrhea).
- **Amoxycillin:** better absorption, higher tissue level & causes no diarrhea (dose 0.25-1 gm / 6 hours).

2. Anti-staph penicillins: (Semi-synthetic)

- **Methicillin, oxacillin, cloxacillin, dicloxacillin, flucloxacillin.**
- **Dose:** 0.25-1 gm/6 hours oral or parenteral (the dose can be increased).
- **Augmentin** (Amoxycillin + Clavulonic acid) inhibits β -lactamases, 375-625 mg / 12 hr, oral or parenteral.
- **Unasyn** (Ampicillin + Sulbactam) 375 mg – 750 mg / 12 hr, oral or parenteral.

3. Anti-pseudomonas penicillins:

- **Carbenicillin** (Pyopen). Others e.g. Azlocillin (1000-5000 mg/6 hr).

4. Benzyl penicillin & related group: for gram (+ve) cocci & bacilli.

Drug	Route	Dose
Benzyl penicillin (<i>penicillin-G</i>)	I.M. & I.V	Up to 20 million units/day
Phenoxymethyl penicillin (Penicillin-V)-(Ospan)	Orally	250-500 mg/6 hours.
Procaine penicillin	I.M. only.	300,000-600,000 units/day.
Benzathine penicillin	I.M. only.	1.2 million unit/2 wks.

5. Imidinopenicillins: active against gram -ve e.g. Mecillinam (Selexid)

Adverse reactions of penicillins

1. Hypersensitivity reactions → urticaria, anaphylaxis.
2. Large doses → encephalopathy (dose related).
3. Gastrointestinal upset.
4. Ampicillin → diarrhea.
5. Methicillin → interstitial nephritis.
6. Drug fever.



Cephalosporins (beta-lactam)

	1 st generation	2 nd generation	3 rd generation
Mechanism	They are similar to penicillins concerning structure & spectrum, so, if a patient is sensitive to penicillin we can use erythromycin rather than cephalosporins to avoid cross sensitivity !?		
Spectrum	Mainly Gm (+ve) & some Gm (-ve).	Gm (+ve) & broader spectrum against Gm (-ve).	Mainly effective against Gm (-ve).
Examples	▪ Cephalexin (Keflex). ▪ Cephadrine (Velosef).	▪ Cefamandole (Mandole). ▪ Cefuroxime (Zinnat) Oral also (250-500 mg / 12 hr).	▪ Cefotaxime (Claforan). ▪ Cefoperazone (Cefobid). ▪ Ceftazidime (Fortum).
Route	Oral or injections.	I.V. or I.M.	I.V or I.M.
Dose	2 gm – 4 gm /day to be ↑ when needed.		
Indications	1. Respiratory tract infections. 2. U.T.I. e.g velosef due to low nephrotoxicity or 3rd generation due to minimal nephrotoxicity. 3. Undiagnosed sepsis. 4. Otitis media. 5. Meningitis → 3rd generation especially cefotaxime.		
Side effects	1. Hypersensitivity reactions as → urticaria, anaphylaxis.... 2. Haemolytic anaemia (immune mediated). 3. Nephrotoxicity is minimal with 3rd generation (the dose can be reduced if creatinine cl. <10)		

Other Beta-lactam agents

- **Imipenem** (Tienem) 1-2 gm/D I.V. infusion.
It acts on aerobic and anaerobic gm +ve and gm –ve organisms.
- **Aztreonam**: Limited to gm –ve including pseudomonas (It is a monobactam).

Macrolides

Mechanism

Bacteriostatic by inhibiting protein synthesis, acting against Gm (+ve) & some Gm (-ve) bacteria.

Indications

1. Strept, staph or pneumococcal infections.
2. Diphtheria, mycoplasma or legionella infection.
3. Prophylaxis against rheumatic fever.

Doses & preparations:

- **Erythromycin** 250-500 mg/6 hours orally, there is a preparation for I.V. injection.
- **Roxithromycin (Rulid)** 150 mg twice/d
- **Recently → Azithromycin (Zithromax)** 250 mg tablet, dose 500 mg/D for 3 days.
- **Clarithromycin (claribiotic)** 500 mg/12 hr.
- **Spiramycin is used in treatment of toxoplasmosis.**

Side effects:

1. Nausea, vomiting & diarrhea.
2. Hypersensitivity reactions as urticaria, anaphylaxis,....



Chloramphenicol

Mechanism Bacteriostatic by inhibiting protein synthesis, acting against many Gm (+ve) & Gm (-ve) bacteria.

Indications

1. Typhoid fever.
2. Bacterial meningitis (if the patient is allergic to penicillin).

Doses & preparations:

- *Thiophenicol, Cidostin.*
- 50 mg/kg/day in divided doses/6 hours.

Side effects

1. Nausea, vomiting & diarrhea.
2. Bone marrow suppression (toxic dose or idiosyncrasy).
3. **Gray baby syndrome** in premature infants & neonates due to failure of the liver conjugation with inadequate renal excretion of chloramphenicol metabolites causing circulatory failure, in which the skin develops a cyanotic grey colour.
4. Hypersensitivity and encephalopathy.

Tetracyclines

Mechanism: bacteriostatic by inhibiting protein synthesis.

Spectrum

- | | |
|----------------------------------|-------------------|
| 1. Gm (+ve) & Gm (-ve) bacteria. | 2. Mycoplasma. |
| 3. Rickettsia. | 4. Coxiella. |
| 5. Chlamydiae. | 6. Some protozoa. |

Indications

- | | |
|----------------------------|-----------------------------------|
| 1. Mycoplasma pneumoniae. | 2. Chlamydia (urethral syndrome). |
| 3. Sinusitis (Vibramycin). | 4. Brucellosis, cholera. |

Doses & preparations

1. **Tetracycline**: 50-500 mg/6 hours oral.
2. **Doxycycline**: 100 mg/day oral (Vibramycin), it is the least toxic.
3. **Demeclocycline** used in SIADH as it decreases the sensitivity of kidney tubules to ADH.

Side effects:

1. Nausea, vomiting & diarrhea.
2. Discoloration of developing teeth.
3. Outdated tetracyclines → Fanconi like \$.
4. Hepatotoxic e.g. fatty liver.



Aminoglycosides

Mechanism Bactericidal by acting on bacterial ribosome & inhibiting protein synthesis.

Spectrum

1. Mainly Gm (-ve) cocci & bacilli.
2. Staph.

Doses, preparations & indications:

1. Streptomycin:

- 1 gm/day I.M. (not > 1-2 months).
- **Used in:** T.B., brucellosis. (It is the least toxic aminoglycoside)

2. Gentamycin (garamycin)

- 5 mg/kg/D (ampole 80 mg).
- **Used in:** proteus, klebsiella, staph,...

3. Tobramycin (Nebcin):

- Same dose & uses as gentamycin.
- **Used also in:** pediatric gastro-enteritis.

4. Neomycin:

- 1 gm/6 hours orally (local action on intestine).
- **Used in:** G.I.T. sterilization e.g. in cases of hepatic encephalopathy.

5. Amikacin (Amikin) → 15 mg/Kg/D.

The dose with impaired renal function. = the dose for patients with normal kidney function divided by S.creatinine.

Side effects:

1. Ototoxicity: cochlear & vestibular. Especially with lasix.
2. Nephrotoxicity: acute tubular necrosis.
3. Hypersensitivity reactions as urticaria, anaphylaxis,....
4. Neuromuscular blockade.

Quinolones

Mechanism Bactericidal via inhibiting DNA synthesis.

Members

- **First generation:** Nalidixic acid (Nigram), oxolonic acid.
- **Second generation:** Pipemidic acid.
- **Third generation:** Norfloxacin, Ofloxacin (Tarivid), Pefloxacin (Peflacin), Ciprofloxacin (cipro), levofloxacin (Tavanic).

Spectrum

- Gm (-ve) organisms.
- New members are active against pseudomonas & Gm (+ve) cocci.



Indications

1. Urinary tract infections (as they are concentrated in urine).
2. Third generation can be used in systemic infections e.g.
pefloxacin (400 mg/12 hours orally),
levofloxacin (250-500 mg/D) and
Ciprofloxacin (500-750 mg twice/d), it is efficient in ttt of typhoid fever.

Ciprofloxacin, levofloxacin, pefloxacin can be given by infusion.

Adverse effects:

1. G.I.T. upset with nausea, vomiting & diarrhea.
2. Hypersensitivity reactions as urticaria, anaphylaxis,....
3. Agranulocytosis.
4. They are avoided in pregnancy, lactation and children as they may cause arthropathies in children.

Vancomycin

Mechanism

Bactericidal, interfering with the bacterial cell wall (like penicillin). So, it can be used in cases of penicillin hypersensitivity.

Dose & spectrum:

- It is active only against Gm (+ve) organisms (**Anti-staph**).
- 0.5 gm/6 hours I.V. in severe staph infections eg. endocarditis.
- It can be used in staph enterocolitis & pseudo-membranous colitis and in methicillin resistant staph aureus (MRSA) infections.

Sulphonamides

I- Non combined sulphonamides

Mechanism:

- Bacteriostatic via competitive antagonism of PABA → block of folic acid synthesis.

Spectrum

- Gm (+ve).
- Chlamydia.
- Gm (-ve).
- Some protozoa.

Indications:

1. Urinary tract infections.
2. Chlamydial infections (trachoma).
3. Prophylaxis against meningococcal meningitis (recently we use Rifampicin).
4. Sulfasalazine used in ulcerative colitis.

Doses & preparations:

1. **Short acting** → sulfadiazine 1 gm/6 hours.
2. **Intermediate** → sulfamethoxazole 1 gm/12 hours.
3. **Long acting** → sulfadoxine.



II- Combined Sulfonamide

Cotrimoxazole (Sutrim) (sulfamethoxazole & trimethoprim).

Mechanism

PABA $\xrightarrow{1}$ dihydro folic acid $\xrightarrow{2}$ tetrahydro folic acid.

Step (1) is inhibited by sulfamethoxazole while step (2) is inhibited by trimethoprim.

Advantages:

- Wider spectrum.
- Bactericidal.

Indications:

1. Urinary tract infections.
2. Respiratory tract infections.
3. Shigellosis.
4. Salmonellosis.
5. Pneumocystis carinii.
6. Trachoma.

Dose:

- 2 tab/12 hours each tablet contains 80 mg trimethoprim + 400 mg sulfamethoxazole.
- Trimethoprim can be used alone (100 mg/12 hrs) in acute UTI, Salmonella and Prostatitis.
- Sutrim infusion is available for pneumocystis carinii.

Other combinations

1. Sulfadoxime + Pyrimethamine for treatment of malaria
2. Sulphadiazine + Pyrimethamine for treatment of toxoplasmosis.

Side effects of sulphonamides:

1. **Hypersensitivity reactions** as urticaria, anaphylaxis,....
2. **GIT upset** with nausea, vomiting.
3. **Haematologic:**
 - Aplastic anaemia.
 - Agranulocytosis.
 - Haemolytic anaemia by acting as innocent by stander or as a hapten.
4. **Crystalluria.**
5. **Kernicterus:** When given in last 2 weeks of pregnancy or to neonates.

Clindamycin (Dalacin-C)

- It belongs to lincosamides group.
- It has a similar spectrum to penicillin against most gm +ve organisms including penicillin resistant staph.
- It is also effective against anaerobes.
- Dose 150 mg – 300 mg / 6 hrs orally or by injection.
- It may lead to pseudomembranous colitis due to over growth of *Clostridium difficile*, which is treated by vancomycin or metronidazole.



Adrenal Corticosteroids & Their Synthetic Analogues

The major glucocorticoid in humans is cortisol (hydrocortisone).

Actions

1. Metabolic effects:

- a. **Carbohydrates** → ↑ gluconeogenesis & ↓ peripheral glucose utilization.
- b. **Proteins** → catabolic effect in C.T., muscle & lymphoid tissue.
- c. **Fats** → ↑ lipolysis, ↑ fat deposition especially on shoulders, face & abdomen.
- d. **Na retention and inceases urinary Ca excretion.**

2. Immunosuppressive & anti-inflammatory:

a. Decrease cell immunity:

- ↓ Lymphocytes.
- ↓ Eosinophils.
- Depression of macrophage function.
- Depression of neutrophil function.

b. Decrease inflammatory response to tissue injury:

- ↓ Histamine.
- ↓ P.G.
- ↓ Release of interleukins from granulocytes.
- Inhibits fibroblastic activity.

3. Other actions:

- a. Increases sensitivity of the cardiovascular system to catecholamines.
- b. CNS → euphoria, psychosis, depression.
- c. GIT → ↑ gastric Hcl and pepsin secretion.
- d. Anti-vitamin D action.

Adverse effects:

- | | |
|--|----------------------------|
| 1. Myopathy, muscle wasting. | 2. Osteoporsis. |
| 3. Peptic ulcer. | 4. Weight gain. |
| 5. Hypokalemia. | 6. Hyperglycemia. |
| 7. Growth retardation in children. | 8. Immunosuppression. |
| 9. Adrenal suppression. | 10. Iatrogenic cushing \$. |
| 11. Depression & psychosis. | 12. Delay tissue healing. |
| 13. Salt & water retension → edema, hypertension. | |
| 14. <i>Hypertension due to:</i> | |
| <ul style="list-style-type: none"> - Salt and water retention. - ↑↑ Renine substrate. - Potentiation of sympathetic. - ↑↑ Atherogenesis. | |



Indications

1. Replacement in acute & chronic adrenal insufficiency.
2. Stimulation of lung maturation in the fetus.
3. Anti-inflammatory, anti-allergic & immunosuppressive, so steroids can be used in:
 - Collagen disorders.
 - Autoimmune disorders.
 - Nephrotic \$.
 - Shock.
 - Organs transplantation.
 - Leukemias, lymphoma (lympholytic effect).

Preparations & doses of glucocorticoids & their equivalent doses

Compound	Trade name	Duration	Glucoc-(anti-inflammatory	Mineralo- (salt & H ₂ O retention)	Equiv. dose
Cortisol (only inj.)	Solu-cortef	Short acting	1	1	20
Prednisolone	Hostacortin-H	Intermediate	4	0.3	5
Prednisone	Hostacortin	Intermediate	4	0.3	5
Methyl-prednisolone	Solumedrol	Intermediate	5	0	4
Triamcinolone	Kinacort	Intermediate	5	0	4
Dexamethazone	Decadron, Deltazone	Long acting	30	0	0.60
Betamethazone	Celestone, Deprofos	Long acting	30	0	0.60

N.B.: Prednisone is converted in the liver to prednisolone, so prednisolone (Hostacortin-H) is preferred in liver disease.

Alternate – day steroid therapy

One of the most effective measures to minimize the cushinoid effects, is to administer the total 48 hour dose as a single dose of intermediate acting steroid in the morning every other day.

Withdrawal of steroid

- This is initiated by an alternate day schedule
- Then gradual withdrawal over weeks
- The dose discontinued after the dose has been reached 5-7.5 mg prednisone. Also we can give ACTH injection (synacthen) to stimulate the adrenal gland.



NSAID (Aspirin like drugs)

Classification

1. **Salicylic acid derivatives:** e.g. Aspirin.
2. **Pyrazolones:** Phenylbutazone, dose 100 mg 3 times/d.
3. **Oxicams:** Piroxicam (Feldene®) 10-20 mg/D.
4. **Acetic acids:** Indomethacin (75 mg/d), Diclofenac Na (Voltaren®) 50-100 mg/D, Diclofenac K (Cataflam®) 50-100 mg/D.
5. **Propionic acid derivatives:** Ibuprofen (Brufen®), Ketoprofen.
6. **Fenamic acids:** Mefenamic acid (ponstan®).

N.B.: Meloxicam 7.5-15 mg/D, it is an anti-Cox II NSAID without gastric irritation.
Examples (Mobic®, Melocam®).

Actions

A. Analgesic action

- Peripherally (anti PG).
- Centrally (thalamic level).

B. Antipyretic action

- Inhibition of pyrogen induced PGE₂ synthesis in the hypothalamus thermoregulatory center.

C. Anti-inflammatory

- Anti PG.
- Inhibition of PNL adhesions and migration.

Side effects

- GIT → PU, Dyspepsia, Heart burn.
- Kidney → (intestinal nephritis).
- Hypersensitivity → Bronchospasm, urticaria.
- Antiplatelets effect.
- Displace Warfarin, Sulpha from plasma proteins.
- Inhibition of renal PG leading to salt and H₂O retention and ↑ K⁺.

Salicylates

- They are derivatives of salicylic acid.
- Synthetic derivatives are Sodium salicylate and Acetyl Salicylic acid or Aspirin.

Actions

1. Analgesic, antipyretic and anti-inflammatory → See NSAID.
2. Blood → low Dose (Antiplatelet).
→ Large Dose (> 5 gm/D) → Hypoprothrombinemia (due to competition with vitamin K).
3. Large dose (> 5gm/d) → ↑↑ uric acid excretion.
4. Local irritant (keratolytic).



Side effects

- GIT → Peptic ulcer, heart burn.
- Allergy → Asthma, urticaria.
- Bleeding tendency.
- Nephrotoxicity.
- Reye's S.
- Salicylism (headache, dizziness, tinnitus).
- Hyperventilation, due to stimulation of respiratory centre.

Preparations

1. *Aspirin* (Acetyl Salicylic Acid).
(Alexoprine = Aspirin + Al hydroxide)
2. *Sodium salicylate*
3. *Salicylate derivatives*
 - Salsalate
 - 5 amino salicylic acid, used for inflammatory bowel disease.

Antiviral Drugs

a. Amantadine

- It inhibits viral replication by inhibition of virus uncoating.
- Used in influenza and parkinson's disease.
- Dose: 100 mg/12 hrs oral.

b. Ribavirin viracure (1000-1200 mg/D)

- It inhibits viral RNA and DNA replication.

Uses

- Inhaler in bronchiolitis caused by syncytial virus in children.
- Oral in virus-C hepatitis in combination with interferon.

c. Idoxuridine

It is pyrimidine analogue used in *H. simplex* keratitis (eye drops).

d. Acyclovir (Zovirax)

- It is a purine analogue.
- Used to treat Herpes simplex and H. zoster.
- Oral 200 mg/ 4 hrs.
- IV 5 mg/Kg/8 hrs.

e. Ganciclovir (cymevene)

It is an analogue of acyclovir with high activity against CMV. IV 5 mg/Kg/ 12 hrs.

f. Zidovudine (retrovir)

It inhibits HIV, replication by competitive inhibition of HIV reverse transcriptase. Dose: 200 mg/ 8 hrs.

g. Interferons (Roferon. Pegasys)

(See Hepatology). They are non specific antiviral, but, they are active only in the species in which they produced (species specific)



Cancer Chemotherapy

a. Alkylating agents

They transfer their reactive alkyl group to the cells inhibiting their function.

- Cyclophosphamide (Endoxan) it causes Hgic cystitis. 1-2 mg/Kg/d oral.
- Chlorambucil (Leukeran), 0.1-0.2 mg/Kg/d oral.
- Melphalan (Alkeran), 6 mg/d.
- Busulphan (Myleran), 2-8 mg/d Orally.

b. Antimetabolites

- Folic acid analogues e.g. Methotrexate 15-30 mg/d orally.
- Pyrimidine analogues e.g. cytosine arabinoside 200 mg/m²/d.
- Purine analogue e.g. 6 MP, 6 thioguanine.

c. Antitumour antibiotics

- Cytotoxic antibiotics e.g (Bleomycin, Adriamycin, mithramycin, mitomycin), they are anti DNA.

d. Hormones

- Steroids, they have suppressant effect on lymphocytes in leukemia & lymphoma.
- Estrogens for cancer prostate.

e. Radioactive molecules

f. Hydroxyurea: In Myeloproliferative diseases, 100 mg/m²/d.

Side effects of cancer chemotherapy

1. BM depression.
2. Inhibition of cellular and humoral immunity.
3. Nausea and vomiting.
4. Gonadal damage.
5. Teratogenisty.
6. Hyperuricemia.
7. Tumor lysis \$ ↑K, ↑P and hyperuricemia → nephropathy (acute renal failure).
8. Induction of malignancies e.g. Acute ML, Non Hodgkên Lymphoma.



HELMINTHS

Trematodes or flukes e.g. *Bilharziasis*, *Fasciola*.

Cestodes or tapeworms e.g. *Taenia saginata*, *T. solium* – *Diphyllobothrium latum*.

Nematodes or round worms e.g. *Enterobius*, *Ascaris*, *Filaria*, *Strongyloides*, *Trichinella*, *Ancylostoma*.

Schistosomiasis

The most important species are:

1. *Sch. haematobium* causing urinary bilharziasis.
2. *Sch. mansoni* causing intestinal-hepatic bilharziasis.
3. *Sch. japonicum* causing small intestinal bilharziasis (in Far East).

Pathology

1. Stage of invasion:

- Cercarial dermatitis: (swimming itch due to penetration of cercaria).
- Cercarial pneumonitis: patchy congestion of the lungs during passage of cercaria through lungs with cough, fever & eosinophilia.

2. Stage of oviposition:

- *Sch. haematobium* in ureter, urinary bladder & seminal vesicles.
- *Sch. mansoni* in submucosa of descending colon and rectum.
- The ova are surrounded by granulomatous reaction (T-cell mediated).

3. Stage of tissue reaction and fibrosis:

- Fibrosis replaces granulomas leading to many complications → see later.

Clinical picture

Urinary	Intestinal
1. Terminal haematuria, (endemic haematuria).	1. Dysentery.
2. Dysuria.	2. Tenesmus & mucus in stools.
3. Frequency.	3. Prolapse of rectal mucosa.
4. Percipitancy.	4. Colonic, rectal & anal polyposis.
5. Loin pain.	5. Anal fissures.
6. ± haemospermia.	6. Anal fistulae.

Schistosomiasis japonicum

The adult worm infects in addition to man, the dog, rat and sheep. The pathology is similar to that of *S. mansoni* but with more extensive and widespread lesions plus neurological lesions.



Complications

A. Urogenital complications:

1. Urethra: stricture and fistula.

2. Urinary bladder:

Cystitis, stone, contraction, calcification and squamous cell carcinoma.

3. Ureter: stone, hydroureter, pyoureter and vesicoureteric reflux.

4. Genitalia:

- a. Male → epididymitis, prostatitis, funiculitis.
- b. Female → granulomas & ulcers in vulva, vagina or Cervix., PID (pelvic inflammatory disease).

5. Kidney:

- Hydronephrosis, pyonephrosis, stone.
- Bilharzial nephropathy:
 - Focal segmental G.N.
 - Mesangio-proliferative.
 - IgA nephropathy.
 - Amyloidosis.
 - Membrano-proliferative.
 - Membranous G.N.

B. Gastrointestinal complications:

1. Colon: prolapse, polyposis, anal fissures, fistulae, strictures.
2. Liver: fibrosis, portal hypertension, late, liver cell failure may occur.

C. General complications:

1. Anaemia.
2. Dwarfism.
3. Sexual immaturity.
4. Clubbing with polyposis.
5. Cardiopulmonary schistosomiasis → see later.
6. Ectopic schistosomiasis → see later.
7. Chronic salmonellosis → see later.

Chronic salmonellosis

	<i>Complicating Sch. haematobium</i>	<i>Complicating Sch. mansoni</i>
Fever	Prolonged, remittent or intermittent.	Prolonged + remittent or continuous.
Symptoms	Dysuria, haematuria.	Abdominal pain.
Signs	Hepatosplenomegaly (HSM) may be present.	HSM, LL edema, ascites, LN.
Blood culture	Salmonella, paratyphi.	
Urine / stools	Bilharzial ova	
Treatment	Sutrim for 10 days + Praziquantal..... see later.	

N.B.: It is suggested that salmonellae can penetrate schistosomes and multiply within their caeca, so schistosomes expelling salmonellae into circulation with intermittent manner.



Ectopic Schistosomiasis

These are specific local reactions to bilharzial worm or their eggs occurring outside the porta-caval venous circulation and the urinary system.

Common ectopic sites:

1. Nervous system:

Picture of focal lesion in the following sites:

- Cerebrum with japonicum.
- Cerebellum with mansoni.
- Spinal cord with mansoni or haematobium.

Schistosomiasis of the spinal cord:

- Myelopathy of spinal cord.
- Intramedullary granuloma → sphincteric disturbances.
- Radiculitis specially in cauda equina.

2. Scrotum → epididymis & hydrocoele.

3. Skin.

4. Eyes → conjunctiva & lids.

Diagnosis of schistomiasis:

1. Risky patient i.e. (living in endemic area).

2. Clinical picture and complications.

3. Investigations:

a. Direct methods:

1. **Urine** → ova (sedimentation or concentration method).
2. **Stool** → ova (sedimentation or concentration method).
3. **Sigmoidoscopy & biopsy (rectal snip):**
 - Congestion, granular sandy patches, ulcers, polyps.
 - Rectal snip showing either living or dead ova.
4. **Cystoscopy & biopsy:** (sandy patches)
5. **Liver biopsy:**
 - Periportal fibrosis.
 - Ova in the portal tracts.

b. Indirect methods: (serology)

1. **Group A:** (they diagnose bilharzial infection and do not indicate activity)
 - Intradermal test.
 - Haemagglutination test.
2. **Group B:** (state of activity & cure after treatment)
 - Circumoval precipitin test (COPT), a drop of the patient's serum is added with living ova, if there is precipitate around the ova = positive test due to presence of bilharzial Abs in the serum.
 - ELISA: It also indicates active infection.

c. Other investigations:

- **Abdominal US** → periportal fibrosis, portal v. dilatation, ascites.
- **Upper GI endoscopy.**
- **Ba enema & proctosigmoidoscopy.**



Treatment

I. General measures:

- Nourishing diet.
- Patient education.
- Treatment of anemia.

2. Anti bilharzial drugs

Drug	Species affected	Dose	Side effects	Remarks
Metrifonate (Bilarcil)	<i>S. haematobium</i>	Single dose of 7.5-10 mg/kg every other week x 3.	Cholinergic symptoms.	
Oxamniquine (Vansil)	<i>S. mansoni</i>	15 mg/kg single oral dose.	Oxamniquine fever.	
Niridazole (Ambilhar)	<i>S. haematobium</i> & <i>S. mansoni</i>	15 mg/kg for 20 days.	Convulsions.	
Praziquantel (Biltricid)	The three species & other parasites as fasciola, <i>H. nana</i> and cysticercosis.	40 mg/kg single oral dose. Tab → 600 mg. the dose can be fractionated into 2 doses separated by not more than 4 hours. The dose can be repeated after 2 weeks.	Mild nausea, vomiting, fever, pruritus.	- Safe in HSM. - Not used in pregnancy & lactation, it should be stopped for 72 hours after treating lactating mother.

Mode of action of praziquantel

- Muscular contraction of the worm due to ↓ K and ↑ Ca influx.
- ↓ ↓ glucose uptake.

3. Other measures:

- polyposis → endoscopic polypectomy.
- Hepatic bilharziasis → discussed later.

Hepatic Schistosomiasis

It is one of the most serious complications of schistosomiasis mainly schistosoma mansoni.

Pathogenesis:

- Prolonged repeated embolization of ova coming from portal tributaries → granulomatous reaction in the portal tracts → periportal fibrosis → presinusoidal portal hypertension.
- Schistosomiasis leads to liver fibrosis not cirrhosis.
- **Bilharzial patients develop cirrhosis very late.....why?**
 - Post hepatic through parenteral route leading to viral hepatitis.
 - Immune reaction!?
 - Associated malnutrition!?

Pathology: (No distortion of hepatic architecture)

- **Fine periportal fibrosis.**
- **Coarse periportal fibrosis.**



Clinical picture:

Symptoms:

- Asymptomatic.
- History of the cause (i.e. intestinal bilharziasis.....).
- Portal hypertension.....
- LCF.....very late with occurrence of cirrhosis.

Signs:

Stages of hepatic schistosomiasis

- 1- Hepatomegaly stage (due to congestion and ova deposition).
- 2- Hepatosplenomegaly stage (spleen is enlarged due to RES hyperplasia + congestion).
- 3- Splenomegaly stage:
 - Firm tender spleen, $\pm$ hypersplenism.
 - Liver is shrunken, firm, nodular, sharp & not tender.
 - Collaterals of portosystemic shunts.
- 4- Ascitic stage: ascites (due to hypoalbuminaemia and portal H).
- 5- Stage of liver cell failure.

Investigations:

1. **Urine & stools** $\rightarrow$ ova.

2. **Blood picture:**

Early: eosinophilia & leucocytosis (active infection).

Late: pancytopenia (hypersplenism).

3. **Liver function tests**: impaired in late cases e.g. $\downarrow$ s. albumin.

4. **Serology**.....

5. **Sonar**: periportal fibrosis, ascites, portal vein dilatation.

6. **Endoscopies**:

- Upper GIT: varices, congestive gastropathy.
- Lower (sigmoidoscopy): rectal snip showing ova.

7. **Liver biopsy**: periportal fibrosis, ova in liver tissue.

Treatment:

- Treatment of Bilharziasis..... if there is living ova or (+ve) serology.
- Colchicine to minimize fibrosis!?
- Correct malnutrition.....
- Treatment of complications.....



Cardio-pulmonary Schistosomiasis

- Cardiopulmonary affection is usually associated with hepatosplenomegaly (some eggs are carried beyond the liver to the lung vessels with portocaval anastomosis i.e. portal H) in cases of sch. mansoni.
- In *Sch. haematobium* → the eggs are already present in the circulation and easily reach to the lungs.
- The disease is more common and more severe with *Sch. mansoni*.
- Eggs, are deposited in the pulmonary arterioles and capillaries → diffuse end arteritis obliterans, this will lead to:
 - Pulmonary hypertension.
 - Core pulmonale (Ayerza's disease).
 - Pulmonary artery aneurysm.
 - This is associated with HSM.
- Lungs may be affected by cercaria in their migration in the invasive stage → **larval pneumonitis**.
- Embolized worms in the lung vessels produce no lesion unless they die → **acute focal necrotizing reaction called verminous pneumonia**.

Dihpyllobothrium latum

It is acquired by ingestion of undercooked fresh water fish; it may lead to vit B₁₂ ↓, treated by praziquantel 20 mg/kg once.

Hymenolepsis nana

- The most common cestode in Egypt specially in children.
- The worm is 2 cm, lives only for few weeks in the proximal part of the ileum.
- Transmitted by feco-oral route.

Clinical picture:

- Usually asymptomatic.
- Massive infection → abdominal cramps, diarrhea & dizziness.
- It is diagnosed by stool analysis for ova.

Treatment: (praziquantel) see later.

Taneia

T. saginata:

- The adult worm lives in the small intestine.
- Mild intestinal symptoms, stool examination For ova, TTT by praziquantel 25 mg/kg one dose.

T. solium:

- Eating of undercooked pork, the worm lives in the small intestine.
- It may lead to human cysticercosis with lesions in skin, skeletal muscles & brain.
- TTT of cysticercosis by praziquantel 50 mg/kg/day in three divided doses for 10 days + steroids + Albendazole 15 mg/kg/day for 8 days.
- T. solium can be treated also with Atebrine.



Fascioliasis

- Fasciola is one of the trematodes.
- The causative worm of the disease in Egypt is fasciola hepatica. It lives in the bile duct.

Clinical picture

- Hepatitis like symptoms in the form of triad (fever, tender hepatomegally and eosinophilia)

Diagnosis

- Finding typical ova in the stools, or serology (ELISA).
- Abnormal liver enzymes (alkaline phosphatase elevated more than transaminases).
- Marked eosinophilia about 30-40 %.

Treatment: See later.

Oxyuris

***Entrobis vermicularis*-Pinworm**

- This helminth is common throughout the world.
- It lives in the large intestine specially the caecum & appendix.

Routes of transmission

- **Direct ingestion of mature ova** via contaminated hands, food and water.
- **Retro-infection:** eggs hatch in the perianal region & larvae migrate back to the bowel.
- Inhalation from air and swallowed from orophaynx.

Clinical picture

1. Asymptomatic.
2. Nocturnal pruritus ani → irritability, insomnia & perianal eczema.
3. Vulvitis & urethritis in females.
4. Pinworms may be seen by the patient.
5. Nocturnal enuresis.

Diagnosis

Applying the adhesive surface of **cellophan tape** to the perianal skin in the morning. This is then examined on a glass slide under microscope.

Treatment (see later)

Each member in the family should be treated during this period, clothes and bed linen are laundered and finger nails must be scrubbed before meals.



Ascariasis

(*Ascaris lumbricoides* - Round worm)

Routes of transmission

Ingestion of embryonated eggs in contaminated water or vegetables. These hatch in the duodenum and the larvae migrate through the lung → bronchial Tree → swallowed → Small intestine (the worm lives in small intestine).

Clinical features

It is characterized by an early pulmonary phase & late intestinal phase.

1. Light infection is asymptomatic.
2. *Ascaris* pneumonitis (**Loeffler's** \$ due to migrating larvae)
 - C/P → fever - cough - dyspnea - wheezing → ASTHMA. → radiologic signs of lung infiltration by eosinophils.
3. Intestinal phase (symptoms due to the adult worm):
 - Abdominal pain or colic.
 - Malabsorption.
 - Intestinal obstruction.

Ectopic ascariasis:

- Large intestine → expelled from anus.
- Back to stomach → vomited.
- Common bile duct → obstructive jaundice.
- Common pancreatic duct → acute pancreatitis.
- Rarely, intestinal perforation → peritonitis.

Diagnosis

- Detection of the ova or even the adult worm in stools.
- Plain X-ray & barium studies showing worms in the small intestine.
- Upper GI endoscopy may show worms in the 2nd part of the duodenum.
- ERCP may show worms protruding from the CBD in cases of obstructive jaundice.

Treatment

- Pulmonary phase: symptomatic treatment.
- Intestinal phase: drugs (see later).



Ankylostomiasis

(*A. duodenale* - Hook worm)

It is a parasite of the human small intestine living in duodenum and upper jejunum. The adult worm is about 1 cm long.

Routes of transmission

1. Larval penetration of the skin when in contact with contaminated soil.
2. Oral ingestion of infective larvae.

Clinical picture

Asymptomatic infection is more common than symptomatic infections.

1. Ground itch: Due to invasion of the skin by larvae.

2. Pulmonary stage: (pulmonary eosinophilia)

- Occurs during migration of larvae through the lung.
- There are dry cough, fever & mild asthmatic wheezing.

3. Stage of established infection:

- Iron deficiency anemia (each worm consumes 0.2 ml blood daily).
- Hypoalbuminemia.

Diagnosis: Ova in stools, ↓ Hb, Eosinophilia.

Treatment: See below + TTT of iron deficiency anemia.

Treatment of Some Helminths

Disease	Drug	Dosage
Oxuris	Mebendazole (vermox)	100 mg tab. 1X2X3 repeated after 10 days.
	Flubendazole (fluvermal)	Dose as vermox.
	Levamisole (ketrax)	5 mg/kg single oral dose.
Ascariasis	Mebendazole (vermox)	1x2x3
	Flubendazole (fluvermal)	Dose as vermox.
	Levamisole (ketrax)	Dose as in oxuris.
Ancylostomiasis	as ascariasis.....	
Hymenolopis nana	Praziquantel	25 mg/kg once, can be repeated one week later.
Fascioliasis	Bithionol	30-50 mg/Kg/d for 2 weeks
	Praziquantel	25 mg/kg TDS for 3 days.
	Triclabendazole (fasinex) given for animal & for human.	10 mg/kg as a single dose



Trichinella

Transmitted to man by eating partially cooked infected pork.

Clinical Picture: (Nausea and vomiting 24-48 hours after infected meal then:

- Fever.
 - Invasion of the diaphragm → cough, dyspnea
 - Stiffness, pain and tenderness in the affected muscles
 - Myocarditis, encephalitis
- } Due to larval invasion

Investigations

Biopsy from deltoid or gastrocnemius + serology.

Treatment

Albendazole 400 mg daily for 6 days + steroids (anti-inflammatory).

Strongyloidiasis

It can be associated with immune suppression, affecting duodenum and jejunum.

Clinical Picture

- Penetration of skin by larvae → itchy rash.
- Worms in gut → abdominal Pain, diarrhea, steatorrhea.
- Allergy → urticaria, wheezing.
- Systemic → pneumonia and meningoencephalitis.

Investigations

Larvae in stool, serology, jejunal biopsy.

Treatment

Albendazole 15 mg/Kg twice daily for 3 days, a second course may be required.

Filariases

I. *Wuchereria bancrofti* (lymphatic filariasis) (The commonest in Egypt)

Life cycle and Pathology

- The adult worms live in the lymphatics → lymphangitis → lymphatic obstruction
- The female gives rise to microfilaria, which are found in the blood with a characteristic nocturnal periodicity.
- Microfilaria are taken from blood by mosquitoes, (*Culex pipiens*) they develop into larvae (which are infective to man) that enter a new person via a mosquito bite.
- Early there is inflammatory phase with fever lymphangitis in lower limbs. Orchitis may occur. This is followed by obstructive phase of lymphatics due to repeated lymphangitis → elephantiasis.



Clinical picture:

- Attacks of inflammation affecting the lower limbs & scrotum with fever (inflammatory phase).
- Edema starting as pitting & ends as non pitting (elephantiasis).
- Hydrocoele.
- Chyluria.
- Chylous ascites, pericardial & pleural effusion.
- Tropical pulmonary eosinophilia can occur

} Obstructive
Phase

Diagnosis

- Detection of microfilaria in mid night blood film, marked eosinophilia.
- Serological tests.

Treatment

- Hetrazan (diethyl carbamazine) 3 mg/Kg t.d.s. for 2 weeks. This course can be repeated twice at interval of 4-6 weeks.
- Antihistaminics or steroid may be used to control allergic phenomena.

II. *Onchocerca volvulus* (River Blindness)

- It leads to blindness, dermatitis & lymphadenopathy.

III. *Loa-Loa*

- It is presented as a short lived inflammatory edematous swelling (calabar swelling) on a limb and sometimes near by joints from time to time. TTT as above for 3 weeks.

IV. *Dracunculaculus medinensis*

- Skin lesions cellulitis due to 2ry infection.

Complications of filaria

1. Elephantiasis.
2. Chylous ascites, pericardial & pleural effusions.
3. Blindness.
4. Lymphadenopathy.
5. Tropical pulmonary eosinophilia (fever, cough and weight loss).
6. Skin lesions → cellulites due to 2ry infection.

Hydatid disease (Cestode)

- The dog is the definitive host, while the cheep is the intermediate host.
- Close contact between an infected dog and human allows human to act as the intermediate host.
- There are cysts in the liver, peritoneum, or in the lung.
- Symptoms of a mass or epigastric discomfort may occur.
- Rupture into peritoneum or biliary tree → abdominal emergency, obstructive jaundice. Anaphylaxis may complicate either event.
- Physical findings are usually absent, the liver and/or an abdominal mass may be palpable.
- Plain abdominal x-ray may show calcification.
- CT gives details on the site and size.
- Eosinophilia is common, antibodies to hydatid can be detected.
- Medical Management: control of dogs, albendazole (penetrate into large cysts).
- Surgical management: percutaneous aspiration, cystectomy, partial hepatectomy.



PROTOZOAL DISEASES

Protozoa are unicellular organisms, larger than bacteria, more complex and often motile.

Giardiasis

- It is a disease of the duodenum & jejunum.
- It is transmitted by feco-oral route.
- The cysts remain viable in water for up to 3 months.
- It affects mainly children; immunosuppressed individuals also can be affected.

Causative organism

Giardia lamblia: the flagellates attach to the mucosa of the duodenum and jejunum causing inflammation.

Clinical picture (I.P about 1-3 weeks)

- Asymptomatic infection may occur.
- Watery diarrhea, nausea, vomiting and abdominal pain.
- Abdominal distension and tenderness on examination.
- Malabsorption → steatorrhea (due to damage of the microvilli).

Diagnosis

- Detection of cysts or trophozoites in the stool, duodenal fluid examined for the trophozoites (string test).
- Jejunal biopsy by Crosby capsule showing giardia on the surface of the epithelium with partial villous atrophy.

Treatment

- Metronidazole (flagyl) 250 mg tab 1X3X7.
- Tinidazole (fasigyn) 2 gm/D one dose repeated after 7 days.

Leishmaniasis

I. Generalized visceral leishmaniasis (Kala azar):

Cause: *L. Donovanii* transmitted by female sandfly or by blood transfusion.

Pathogenesis: the organism multiplies in monocytes present in the liver, spleen, intestinal mucosa, bone marrow & lymphoid tissue.

Clinical picture: (I.P 1-2 months)

- Enlarged liver, spleen becomes enlarged massively. Also there is lymphadenopathy.
- Anemia.

Diagnosis:

- Stained smears or culture of bone marrow, LN, liver, or spleen.
- Detection of Ab by ELISA & immunofluorescence.

Treatment

- Antimonials (meglumine antimoniate) 20 mg/Kg IV or IM for 20-30 days.
- Amphotericin B and pentamidine can be used.



2. Cutaneous leishmaniasis (oriental sore):

Clinical picture: ulcers that heal by fibrosis, commonly on the face.

Diagnosis: smear from the lesion to be stained by Geimsa stain.

Treatment: same as visceral type.

Toxoplasmosis

It is a worldwide infection caused by *Toxoplasma gondii*.

Transmission

- **Vertical:** from infected mother to fetus.
- **Ingestion of cysts** excreted in the feces of infected cats, or eating under cooked beef or lamb. Ingestion of raw milk from infected goat.
- **Blood transfusion (infected leucocytes).**

Clinical picture

Congenital infection: (transplacental)

- Abortion or still birth.
- Hydrocephalus or microcephalus + cerebral calcification.
- Convulsions & psychomotor retardation.
- Generalized lymphadenopathy.
- Myocarditis.
- Hepatosplenomegally & jaundice.
- Affection of the eye:
 - Cataract.
 - Optic atrophy.
 - Chorioretinitis.

Acquired infection:

- Lymphadenopathy, pneumonia with fever may occur.
- Chorioretinitis & uveitis.
- Lymphocytosis with atypical mononuclear cells.
- May occur in immunocompromised patients.

Diagnosis

1. Detection of Abs by ELISA (IgM) indicates acute infection.
2. Lymph node biopsy.
3. Toxoplasmin test (I.D. injection of toxoplasmic Ag).
4. Toxoplasma may be found in the CSF of immunocompromised patients



Treatment

1. Sulphadimidine 1 g/6 h + pyrimethamine 25 mg/d with folic acid 10 mg/d for 4 weeks (pyrimethamine is a folic acid antagonist).
2. If there is chorioretinitis, corticosteroids can be given.

If toxoplasma occurs in the first trimester, abortion should be considered.

Newly born infants of suspected mothers should be tested by detection of IgM.

Malaria

It is caused by 4 human species:

- *Plasmodium falciparum* → malignant subtertian malaria (periodicity every 24 hrs i.e. every day).
- *Plasmodium vivax & ovale* → benign tertian malaria (periodicity every 48 hrs i.e. every third day).
- *Plasmodium malariae* → quartan malaria (periodicity every 72 hours i.e. every fourth day).

Modes of transmission:

1. Natural route by anopheles mosquito bite.
2. Blood transfusion or drug addicts.
3. Congenitally via the placenta.

The above 2 & 3 will not lead to chronic malaria as no tissue forms are produced, but only erythrocytic stages causing one clinical attack to be treated by schizonticidal drugs only.

Life cycles

1. Asexual cycle (in man = intermediate host):

Pre-erythrocytic (exo-erythrocytic)	Erythrocytic stages
Responsible for chronicity & relapses.	Responsible for the acute attack.
Caused by the natural route only.	Caused by all means of infection.
Treated by 8 amino-quinolines (causing eradication of infection).	Treated by schizonticidal drugs as 4 amino-quinolines, quinine, pyrimethamine leading to cure of the clinical attack.

2. Sexual cycle in mosquito (definitive host):

The mosquito ingests the blood containing microgametocytes (male) & macrogametocytes (female) → unite in the stomach → zygote → penetrates wall of gut → sporozoites → migrate to salivary glands → injected to man (by biting).



Clinical picture

Incubation period: about 10 days.

Stages:

Cold stage (1-2 hours):

- Sense of severe coldness, rigors & vomiting.
- Rectal temperature is rapidly rising to 40° C.
- Skin is cold, with rapid weak pulse.

Hot stage (3-4 hours): (The patient feels very hot)

- Congested face, hands & skin with intense headache & thirst.
- Then temperature starts to fall, pulse is rapid & full.

Sweating stage (2-4 hours):

- Severe sweating.
- Temperature falls to normal & the patient feels exhausted.

NB: There is tender splenomegaly during the paroxysm.

Complications (mainly due to *P. falciparum*)

1. Hemolytic anemia (chronic anemia may occur).
2. Acute renal failure due to hemolysis.
3. Nephrotic syndrome (membranous G.N by *Pl. malariae*).
4. Black water fever: fever, hemolysis & dark urine (hemoglobinuria). This occurs as a complication of malignant malaria due to inadequate antimalarial therapy (intravascular hemolysis of RBCs).
5. Cerebral malaria: headache, coma, no fever or severe hyperpyrexia.
6. Gastro-intestinal malaria: nausea, vomiting, diarrhea.
7. Splenic rupture, tropical splenomegaly.
8. Hyperpyrexia.
9. Pigment gall stones.
10. Algid malaria i.e. watery diarrhea or dysentery.
11. Liver: jaundice.
12. Lung: pulmonary edema.

Investigations

1. Demonstration of the parasite: Blood film (thick drop method).
2. Bone marrow & spleen puncture may show the parasite.
3. Therapeutic test i.e. fever responds to antimalarial drugs.

**NB:**

- Causes of anemia in malaria are:
 - Haemolysis.
 - Dyserythropoiesis.
 - Depletion of folate.
 - RBCs sequestration by the enlarged spleen.
- If blood film is -ve, provocation can be done by examination blood film after adrenaline s.c. injection (0.5 ml 1/1000).

Treatment**A. Chemoprophylaxis:**

1. **Antimosquito measures:** nets, insecticides,.....

2. **Suppressive doses of antimalarial drugs:**

- If Chloroquine resistance present {
 - Chloroquine 500 mg once/week + proguanil 200 mg/D starting 2 weeks before entering endemic area, while there & for 4 wks after leaving.
 - or Mefloquine 250 mg once/week, starting one week before entering the endemic area, while there & for 4 wks after leaving.
- If Chloroquine resistance absent → chloroquine only as above

B. Curative measures:

1. **Schizonticidal drugs:** Destroy the asexual erythrocytic forms.
(ttt of acute attack)

- **Chloroquine (aminoquinolines).**
 - Used for chloroquine sensitive malaria.
 - 600 mg then 300 mg after 6 hours then 150 mg/12 hr for 3-7 days
 - Injections may be used in malignant malaria.
 - Toxicity: anorexia, nausea, vomiting, corneal opacity & retinopathy with optic neuritis.
- **Quinine: (*P. falciparum* is a chloroquine resistant)**
 - 600 mg t.d.s. for 3-5 days. Used in *P falciparum* from chloroquine resistant area.
 - Toxicity: vomiting, deafness, abortion & hemolysis.
 - This regime should be followed by single dose of 1.5 gm sulfadoxine + 75 mg pyrimethamine.
- **Mefloquine: (Alternative to quinine)**

Used also for resistant cases, 500 mg 8 hourly for three doses.



2. Eradication of infection: (for p vivax, malariae and ovale)

- **Primaquine (8-aminoquinolines):**

- Destroys exo-erythrocytic stages, this prevents relapses. (15 mg/d for 14 days).
- Toxicity: abdominal pain, vomiting, hemolysis may develop in cases of G6PD.

NB: P. falciparum requires no additional therapy as there is no exo-erythrocytic stage.

Treatment of complications:

1. Black -water fever:

- Corticosteroids.
- Blood transfusion.
- Antimalarial drugs.

2. Cerebral malaria:

- Parenteral antimalarials (chloroquine 5 mg/kg + 20 ml saline I.V. slowly. The dose should be repeated after 12 hours).
- Packed RBCs & fluids.
- Corticosteroids e.g. 10 mg dexamethasone I.V.

Tropical Splenomegaly Syndrome

- It is an exaggerated immune response to malaria in which there is overproduction of IgM aggregates which are phagocytosed by RES in the spleen and liver, this can be demonstrated by liver biopsy.
- Anemia, lymphocytosis can be confused with leukemia.
- Portal hypertension may develop.
- TTT → 100 mg proguanil/d plus folic acid 5 mg/D, splenomegally and anemia usually resolve over period of months of continuous treatment.



BACTERIAL INFECTIONS

Food poisoning

I- Staph Food Poisoning (Toxin mediated)

It is a non invasive gastro-enteritis caused by thermo-stable *enterotoxin*.

Mode of infection (frequently from a food handler)

- Food contaminated by the organism from respiratory discharge or from a septic lesion on the hand of a food handler.
- Important foods are milk, cream, cakes and cheese favour the growth of staph aureus.

Incubation period: 2-6 hours.

Clinical picture:

- Vomiting initially then severe abdominal colics, diarrhea $\pm$ low grade fever.
- Symptoms persist for few hours then recovery takes place.

Diagnosis: isolation of the organism from food remnants.

Treatment: supportive with I.V or oral fluids to avoid dehydration.

...NB... Vomiting within 1/2 hour after meal suspect allergy (specially seafood) or chemical.

II- Salmonella Gastroenteritis (Non toxin mediated)

The most common forms of salmonellosis are acute gastroenteritis & enterocolitis.

Causative organism:

- *Salmonella typhimurium*.
- *S. enteritidis*.

Mode of infection:

- Ingestion of undercooked chicken or undercooked or raw eggs.
- Carriers who are food handlers are a source of infection.

Incubation period: 12-48 hours.

Clinical picture:

1. Headache, malaise followed by nausea, vomiting, diarrhea & colic.
2. The illness is septicemic as the organism is invasive.
3. It is self-limiting within 2-5 days.



Diagnosis: stool culture.

Treatment:

- Supportive with fluid therapy.
- No antibiotics & no antidiarrheal drugs to wash the infection.
- Sutrim or Ciprofloxacin in severe or prolonged symptoms.

III- Botulism (Toxin mediated)

It is a rare type of bacterial food poisoning due to ingestion of *Clostridium botulinum* toxin.

Incubation period: 12-36 hours.

Source of infection

- Canned alkaline food.
- Preserved fish.
- In such foods, spores germinate under anaerobic conditions → vegetative forms → grow & produce toxin.
- The toxin is destroyed by heating for 20 minutes at 100° C.

Pathogenesis

Exotoxin blocks release of acetylcholine at motor end plate → flaccid paralysis.

Clinical picture

Vomiting initially but no other GIT symptoms, then neurological manifestations as:

- Diplopia (paresis of ocular muscles).
- Dysphagia (paresis of pharyngeal muscles).
- Dyspnea (paresis of respiratory muscles).
- Dysphonia (paresis of laryngeal muscles).
- Paresis of skeletal muscles.

Diagnosis

- Toxin demonstration in stool, vomitus, food remnants & rare in blood.

Management

- Clear airway, ventilation.
- Gastric wash.
- Trivalent antitoxin 20 ml I.V followed by 10 ml 2-4 hours then every 12-24 hours as necessary.
- Guanidine hydrochloride 15-40 mg/kg, it improves the paralysis by reversing the neuromuscular block.



Causes of food poisoning

Infective

1- Non toxin mediated

- Salmonella. - Helicobacter.
- Bacillus anthracis (anthrax).
- Listeria causing meningitis.

2- Toxin mediated

- Staph aureus. - Botulism.
- E-coli (verocytotoxin) produced by E-coli enterohaemorrhagic.

Non infective

1- Allergic

- Shellfish, strawberries.

2- Non allergic

- e.g. chemicals & metals (in cooking pots).

Salmonella infections

Forms of infection

1. Enteric fever.
2. Septicemia.
3. Salmonella gastro-enteritis (food poisoning).
4. Chronic salmonellosis, endemic in Egypt in bilharzial patients.
5. Metastatic lesions e.g. osteomyelitis, liver abscess, brain abscess.
6. Asymptomatic carrier state.

Enteric fever (Enterica-Typhoid fever)

Causative organism: Salmonella typhi & paratyphi A, B.

Mode of infection:

- Feco-oral (contaminated food especially poultry).
- It resists freezing so it can be transmitted by ice-cream.
- Food handlers (carriers).

Pathogenesis:

- Infection begins when organisms penetrate the intestinal wall and invade mesenteric lymph nodes and the spleen. Bacteremia occurs and the infection then localizes principally in the lymphoid tissue of S.I. (Peyer's patches) which become inflamed and may ulcerate, perforate or bleed. The organism may disseminate to the lungs, gall bladder, kidneys or C.N.S.
- The organism appears in feces during 2nd & 3rd weeks.
- The organism may be excreted in urine.

Incubation period: 10-14 days.



Clinical picture:

1st week:

- Gradual onset of malaise, lethargy, headache, anorexia & constipation.
- Temperature rise in a **STEP LADDER** fashion with relative bradycardia.
- Diarrhea and vomiting may prominent early.
- At the end of this week slight tenderness in the hypochondrium may occur and the spleen may be palpable.

2nd week:

- The temperature remains raised (remittent or continuous).
- Rose spots on trunk fade on pressure (It may also appear at the end of the first week).
- The abdomen becomes more distended, the spleen becomes larger. Diarrhea may occur.

3rd week: (The patient may be very ill unless the disease is modified by Ab therapy).

Favorable cases:

- Temperature & toxemia are decreased.
- Abdominal symptoms subside & appetite returns to normal.

Unfavorable cases:

- Symptoms increase in severity → profound toxemia, delirium may occur this is known as **TYPHOID STATE**.
- Intestinal perforation or haemorrhage may occur.

Diagnosis:

History & clinical examination.

Investigations:

1- 1st week → blood culture.

2- 2nd & 3rd week

- Stool culture on enrichment medium as selenite broth or tetrathionate.
- Urine culture on Maconkey's medium.

3- Widal test: (difficult to interpret but very high or rising titre is diagnostic)

- It is best done after 10 days from the onset of the disease.
- It measures serum antibodies against the O and H antigens. Titre > 100 is positive.

4- Blood picture:

- Leucopenia with relative lymphocytosis.
- Leucocytosis with intestinal perforation and peritonitis.

5- Mild rise of ALT & AST.



2. Specific measures:

- Chloramphenicol 50 mg/kg/24 hours (divided 6 hourly) for 2 weeks (old fashion therapy).
- Ceftriaxone (Rocephin) a third generation cephalosporion 50 mg/kg as a single daily dose for one week.
- Amoxicillin 100 mg/kg/D (divided 6 hourly). It can be combined with sutrim.
- **Ciprofloxacin** 500 mg/12 hrs for 2 weeks (**the best**), we can start with injection until clinical improvement then continue with oral route.

Treatment of complications:

- Hemorrhage: blood transfusion, nothing by mouth & antishock measures.
- Perforation: surgery.

- Enemas or laxatives are contraindicated in cases of constipation as they may predispose for hge or perforation.
- Relapse occurs in 10-15 % of cases.
- The chronic carrier should be treated for 4 weeks with 750 mg/12hour ciprofloxacin, cholecystectomy may be necessary in some case.
- Paratyphoid A, B, the course of disease tends to be shorter and milder but with abrupt onset less intestinal complications.

Diphtheria

In many parts of the developing world diphtheria is an important cause of illness. Its incidence has fallen following widespread active immunization.

Causative organism:

Gram (+ve) pleomorphic rod *Corynebacterium diphtheria*.

Mode of infection

- Direct: droplet infection, from cases or carriers.
- Indirect: contaminated fomites.

Incubation period: 2-7 days.

Clinical picture

The organism remains localized at the site of infection with absorption of a soluble exotoxin which damage heart and nervous system.

1. Pharyngeal diphtheria:

- Severe prostration, constitutional symptoms & low grade fever 38°C. it may be high if complicated by infection with other bacteria.
- Greyish membrane appears (necrosed epithelial cells, fibrin, inflammatory cells & RBCs) with pharyngeal & tonsillar inflammation.
- The membrane bleeds easily if scraped.
- Bull neck (cervical lymphadenopathy in severe cases).

2. Laryngeal diphtheria: husky voice, brassy cough with danger of respiratory obstruction.

3. Nasal and cutaneous diphtheria are rare forms.



Diagnosis (It is made on clinical ground as the therapy is urgent).

1. Culture of a portion of membrane on *Löffler's medium* or *blood tellurite*.
2. **Shick test:** detects the immune status of the patient.
Intradermal injection of toxin, absence of reaction means immunity.

Complications

1. Respiratory:

- a. Laryngeal obstruction due to extension of the membrane & edema of respiratory mucosa.
- b. Lung collapse due to inhalation of a piece of the membrane.
- c. Bronchopneumonia due to 2^{ry} infection.

2. Cardiovascular: (death from respiratory failure may occur)

- a. Myocarditis.
- b. Arrhythmia.
- c. Heart failure.

3. Paralytic:

a. Palato-pharyngeal paralysis:

Usually in the second week with nasal voice, dysphagia & nasal regurgitation.

b. Ocular paralysis:

- Diplopia (6th nerve paralysis).
- Loss of accommodation (3rd nerve paralysis).
- Squint (strabismus).

c. Peripheral polyneuritis.

4. Renal: Toxic nephritis.

5. Cutaneous: Purpuric skin eruption in malignant cases.

Treatment

Prophylaxis

- Active immunization for all children.
- Contacts should receive erythromycin and toxoid (immunization).

General measures:

Bed rest, isolation, IV fluids and observation.

Specific treatment:

1. Antitoxin:

- To be given early (once diphtheria is diagnosed clinically) to prevent further fixation of toxin to tissue receptors.
- Dose: 20000-100000 unit IM.

2. Antibiotics:

- Erythromycin or Penicillin G.
- They are given till three consecutive throat swabs are (-ve).

3. Toxoid:

- After recovery full course of immunization should be given.

Treatment of complications: (cardiac, pulmonary & neurological).



Brucellosis

(Undulant fever – Malta fever – Mediterranean fever)

Causative organism: 3 species of gram (-ve) brucella:

1. *B. abortus* from cattle.
2. *B. melitensis* from goats or sheep (the most virulent, it is the main cause in Egypt).
3. *B. suis* from pig.

Epidemiology: farmers, butchers & veterinarians (occupational disease).

Mode of infection:

- Direct contact with diseased animals or their tissues.
- Indirect ingestion of unpasteurized milk or cheese from cows & goats.

Incubation period: about 3 weeks

Clinical picture:

Acute brucellosis:

- Insidious onset, with malaise, headache, myalgia and night sweats.
- The fever is undulant (undulating over 7-10 day periods), continuous or intermittent patterns are frequent.
- Hepatosplenomegally and backache (spinal tenderness) may be present.
- Complications (see below) may occur especially with *B. melitensis* or *B. suis*.

Chronic brucellosis:

- Easy fatigue and myalgia.
- Bouts of low grade fever and sweating for several months.
- Lymphadenopathy with enlarged liver and spleen are usually found.

Localized brucellosis:

- The condition is uncommon.
- Bone and joints, spleen, endocardium, lung, nervous system and urinary tract may be involved.
- Diagnosis by culturing the organisms from the involved site.

Diagnosis

1. **Blood culture or B.M culture:** at least 3 samples during fever spikes.
2. **Brucella agglutination test:** (+ve) from 2nd week. High IgM by ELISA.
3. Leucopenia with relative lymphocytosis.

Complications:.....itis.

1. **CNS:** meningitis, encephalitis, neuritis, paraplegia.
2. **Bones & joints:** spondylitis, osteitis, arthritis, bursitis, osteomyelitis.
3. **Pulmonary:** bronchitis, bronchopneumonia, pleural effusion.
4. **Cardiac:** endo & myocarditis.
5. **Genital:** epididymo-orchitis.
6. **In severe cases** purpuric skin eruption & hge from mucus membrane may occur.



Treatment:

Prophylaxis:

- Sanitation of milk & its products.
- Hygiene education for handlers of infected animals.

General measures:

1. Bed rest during the acute stage.
2. Light diet & vitamins.
3. Symptomatic treatment.

Specific treatment:

1. Tetracycline 0.5 gm/6 hours orally + Rifampicin 600 mg/d for 4 wks.
2. Streptomycin 1 gm/day IM, may be used instead of Rifampicin.

Treatment of complications

Cholera

It is a severe acute gastrointestinal infection caused by *Vibrio cholera*. It is an infectious epidemic disease, transmitted by faeco-oral routes.

Pathology

- The organism multiplies in SI → Enterotoxin → stimulate adenylyl cyclase → secretory diarrhea → severe dehydration.
- There are: acidosis, ↓ Na⁺, ↓ K⁺.

Incubation period: few hours to 5 days.

Clinical picture

- Severe diarrhea without pain or colic.
- Rice water diarrhea (water + mucous).
- Dehydration → hypovolemic shock.

Cholera Sicca: Occurs in which the loss of fluid into the dilated bowel kills the patient before typical gastrointestinal symptoms appear.

Complications

- Acidosis, ↓ Na, ↓ Ca.
- Over TTT → pulmonary edema.

Diagnosis

- Culture of stool, rectal swab are used to isolate the organism.
- Rapid methods e.g. fluorescent antibody technique of stools.



Differential diagnosis

- Bacillary dysentery.
- Food poisoning.

Treatment

- IV fluid.
- Three days TTT with tetracycline 250 mg/6 hrs or co-trimoxazole to reduce the duration of excretion of *Vibrio* and the volume of fluid needed for replacement.

Prevention

- Personal hygiene.
- **Vaccinations:** Limited protection (**Koll's vaccine**) heat killed, 2 doses S.C injection.
- **Chemoprophylaxis:** by tetracycline.

Plague

The disease limited to rodents with sporadic human cases.

Organism: *Yersinia pestis* (Gm -ve bacilli).

Spread:

- Between rodents by their flea. If domestic rats become infected, infected fleas may bite man.
- In the late stages of human plague spread between human occur by droplet infection.

Pathology

- Organism → skin → LN → septicemia → shock → DIC may result.
- Inhalation → alveolar damage.

Incubation period: 3-6 days.

Presentations

- **Bubonic plague:** Commonest, fever, LN (commonly inguinal), toxemia, and splenomegally.
- **Septicemic plague:** acute fulminant infection with shock & DIC.
- **Pneumonic plague:** cough with bloody sputum, dyspnea, cynosis.

Diagnosis:

- Aspirate from LN, sputum, organism stained by M. blue.

Treatment:

- Streptomycin IM 30 mg/kg/D for 10 days or tetracycline 2-3 gm/D for 2 weeks.
- TTT of shock and DIC.

Prevention

- Control of flea.
- Rats control.
- Killed vaccine for those at occupational risk.
- Contacts protected by tetracycline 2 gm/D or sutrim one tab/D for 1 wk (chemoprophylaxis).

Leptospirosis (Weil's Disease)

Organism: gm -ve *Leptospira icterohaemorrhagiae*.

Mode of infection:

- From rodents and other wild animals.
- The organism is excreted in the animal urine and enters the host through a skin abrasion or through intact mucous membranes.
- Certain occupational group are at risk e.g. veterinarians, abattoir workers, sewer workers and those who take part in water sports.

IP: about 10 days.

Clinical Picture:

1- The leptospiraemic phase lasts for about one week ch.ch. by fever, headache, myalgia, suffusion of the conjunctivae, arthralgia, hepatosplenomegaly, LN + skin rash.

2- Immune phase (few days)

- Meningism.
- Tender liver.
- Jaundice.
- Haemolytic anaemia.
- Oliguric renal failure + microscopic haematuria.
- Arrhythmia and heart failure.

Investigations

- Polymorpholeucocytosis.
- Blood culture or CSF culture during the first week.
- Organism in urine in the 2nd week and for 2-4 weeks.
- PCR (blood, CSF or urine).
- IgM Ab.

Treatment

- Penicillin G, 1.5 million units/6 hours for 1 week.
- Tetracycline can be used e.g. Doxycycline 100 mg/12 hrs for 1 week.
- ***Chemoprophylaxis:*** doxycycline for short term prevention.

Anthrax

Etiology: *Bacillus anthracis*, it is transmitted through direct contact with an infected animal e.g. in farmers, butchers.

Clinical Picture: I.P is 1-5 days.

Cutaneous form:

This is the most common mode of presentation, there is erythematous maculopapular painless lesion → ulceration.

Respiratory (Woolsorter's disease):

It is due to inhalation of spores results in a non productive cough, fever. Pleural effusion is common.

Gastrointestinal anthrax:

This presents as gastroenteritis, hematemesis and bloody diarrhea.

Diagnosis:

- Demonstrating the organism in smears or by culture.
- ELISA.

Treatment:

- Phenoxymethyl penicillin 500 mg four times daily for 2 weeks.
- Erythromycin, chloramphenicol and tetracycline can be used.
- Vaccination of exposed workers is effective.

Clostridial Infections

Clostridium is a gram-positive, spore-forming, obligatory anaerobic bacillus.

Tetanus

- It occurs due to wound contamination by *C. tetani* in non-immunized individuals.
- The clinical manifestations are due to a neurotoxin (tetanospasmin), the organism is not invasive.

Clinical features: (I.P varies from a few days to several weeks).

1- Generalized tetanus (the most common form):

- Initially there is trismus (lock jaw) due to masseter muscle spasm then spasm of fascial muscles (risus sardonicus), the spasms occur spontaneously but may precipitated by noise or by light.
- Respiratory distress due to laryngeal spasm.
- Oesophageal and urethral spasm lead to dysphagia and urinary retention.
- Arching of the neck and back muscles (opisthotonus).
- Autonomic dysfunction e.g. tachycardia, arrhythmia and sweating.
- Patients with tetanus are mentally alert.

2- Localized tetanus:

- Pain and stiffness in the muscles surrounding the site of the wound.

3- Cephalic tetanus:

- This occur when the route of entry is the middle ear, cranial nerve lesions specially facial nerve are usual.

4- Neonatal tetanus: (Infection of the umbilical stump).



Diagnosis (it is mainly clinical)

- C. tetani may be isolated from wounds.
- Phenothiazine over dosage, meningitis and tetany are similar conditions.

Treatment:

- I.V penicillin G 10-12 million units/D for 10 days + human antitetanus immunoglobulin 150 units/kg I.M.
- Diazepam to control spasm, B-Blockers for autonomic dysfunction.
- Respiratory support.
- Active immunization after recovery.

Prevention:

- 2 doses of 0.5 ml of the toxoid I.M at 8 week interval then a booster dose is given 6-12 months later.
- It is indicated in those who work in a contaminated area e.g. farmers. Also it is given for all women of child bearing age.

Gas gangrene

- It is caused by C. perfringens.
- It occurs in lacerated wounds particularly if there a decreased vascular supply and anaerobic conditions.
- Initially there is pain then oedema at the injury site.
- The part distal to the injury becomes cold and pulseless in the affected limb.
- Late the affected muscles are gangrenous with toxemia.
- The characteristic crepitus is also a late feature.
- Hypotension, renal failure and hepatic failure are terminal events.

Treatment

- Surgical debridement with parenteral penicillin and another antibiotic to cover aerobic and anaerobic organisms.

Pseudomembranous colitis

- It is caused by C. difficile few days after antibiotic therapy especially clindamycin. Diarrhea and abdominal pain are usual. It is diagnosed by sigmoidoscopy and identification of the toxin in stool.
- It is treated by stopping any suspected antibiotic – plus vancomycin 125 mg/6 hours orally for 10 days. Metronidazole is also effective and less expensive.

Botulism → see before

Clinical conditions caused by *Staph aureus*.

- **Skin:** furuncles, cellulitis, impetigo and carbuncles.
- **Lungs:** pneumonia and lung abscess.
- **Heart:** pericarditis and endocarditis.
- **CNS,** joints and bone: Meningitis, brain abscess, arthritis and osteomyelitis.
- **Due to toxin:** food poisoning and toxic shock syndrome.

Toxic shock syndrome (TSS)

TSS occurs in menstruating women using tampons. It is manifested by fever, diffuse macular erythema, vomiting, diarrhea, myalgia and shock. Blood cultures are negative, anti TSS are present. Treatment is supportive plus antibiotics.



Diseases caused by *Streptococci*

- **Skin:** impetigo, erysipelas and cellulites.
- **Pharyngeal:** pharyngitis, tonsillitis.
- **Pulmonary:** pneumonia, empyema.
- **Others:** meningitis, endocarditis, lymphangitis and osteomyelitis.
- **Non-suppurative:** Rh fever, G nephritis and scarlet fever.

Scarlet fever: (the organism produces erythrogenic toxin)

- I.P (2-4 days).
- There is pharyngitis, fever then rash on the second day which blanches on pressure.
- The face is flushed with circumoral pallor, also there is strawberry tongue.
- It is diagnosed by throat swabs and elevated ASOT.
- It is treated by penicillin V 125 mg/6 hours for 10 days.

Erysipelas

- It is an acute skin lesion occurs in debilitated and immunosuppressed patients.
- It is manifested by erythematous skin lesion, usually on the face with raised edge.
- Regional lymphadenopathy is common.
- High mortality with bacteremia.
- Penicillin is rapidly effective.

Infections due to *Rickettsia* and *Rickettsia* Like Organisms

1- Epidemic typhus (*R. prowazekii*)

- Fever, headache and measles like eruption are usual.
- Also meningo-encephalitis, splenomegally, pneumonia, myocarditis and renal failure may occur.

2- Endemic (murine) typhus (*R. mooseri*)

- It is a rat infection transmitted to human by rat flea, the disease resembles epidemic typhus but much milder.

3- Rocky mountain spotted fever (*R. rickettsii*)

- Clinical features similar to epidemic typhus with shorter I.P.

4- Scrub typhus (*R. tsutsugamushi*)

- It is similar to epidemic typhus with an abrupt febrile illness, signs in the chest are minimal.

Diagnosis and treatment of rickettsial diseases

- Diagnosis by the indirect fluorescent Ab (sensitive).
- The weil-felix agglutination test is not accurate.
- Treatment by tetracycline 500 mg/6 hours for 7 days.

Q Fever (*coxiella burnetii*, rickettsial like)

- Spread to human by dust, milk from infected cows.
- It is manifested by pneumonia, endocarditis and uveitis.
- It is diagnosed by complement fixation tests
- It is treated by tetracycline.

VIRAL INFECTIONS

Infectious Mononucleosis (Glandular fever)

Causative organism: Epstein Barr virus (EBV).

Incubation period: 7-10 days.

Mode of infection: Oral contact with exchange of saliva (kissing). As the virus replicates in β lymphocytes and shed in the throat.

Clinical picture: (teenagers and young adults).

1. Fever, malaise, headache and anorexia.
2. **Lymphadenopathy:** cervical & axillary LN, may be generalized.
3. **Sore throat**, this is the presenting symptom, there is enlarged tonsil often covered by an extensive white membrane with inflammatory edema of fauces.
4. *Pin pointed petechiae at the junction of the hard & soft palate.*
5. **Spleen:** moderately enlarged in 50 %.
6. Liver: may be enlarged with jaundice.
7. Maculo-papular rash (with intake of ampicillin see complications).

Diagnosis:

1. Blood picture:

- Atypical lymphocytosis.
- Haemolytic anaemia and thrombocytopenia are rare complications.

2. Paul Bunnell & mono spot tests are (+ve) in 90 % of cases.

- Sero(-ve) IMN means (-ve) Paul Bunnell test.
- If you diagnose IMN with -ve Paul Bunnell it is either seronegative or CMV (Differential Diagnosis).

3. ELISA for detection of IgM & IgG antibodies.

Differential Diagnosis

1. Toxoplasmosis.
2. Cytomegalovirus infection.
3. Other causes of sore throat.
4. Acute leukemia.



Complications:

1. Airway obstruction from pharyngeal or paratracheal adenopathy.
2. Cardiac complications: pericarditis & myocarditis.
3. Hematologic complications: autoimmune hemolytic anemia, thrombocytopenia.
4. Neurologic complications with encephalitis and meningitis.
5. Rupture of spleen with trauma of the abdomen.
6. Remote complication e.g. **Burkitt's lymphoma**.
7. Chronic fatigue syndrome.
8. Hepatitis.

Treatment

- Acyclovir or Ganciclovir may be effective.
- Never to prescribe antibiotics specially ampicillin as the patients are very liable to drug eruption (maculo=papular rash) in 90% of patients who have received ampicillin.
- Treatment of complications.
- Steroids, prednisolone 10 mg/ 6 hrs for severe tonsillar enlargement causing dysphagia or difficulty in breathing.

Prognosis

It is a self-limiting disease with good prognosis except rupture spleen which is a serious complication.

Cytomegalovirus infection

1. Congenital disease: rapid onset of jaundice after birth with hepatospleno-megaly, purpura & signs of encephalitis.

2. Acute acquired disease (In immunocompetent person):
similar to IMN but pharyngitis is minimal.

3. Generalized systemic disease (In immunosuppressed patient):

- Occurs in immunocompromised patients specially AIDS.
- Manifested by pneumonitis, hepatitis & leucopenia with lymphocytosis, retinitis especially in cases of AIDS.

Treatment:

Only symptomatic. In serious infections in immunosuppressed patient, we give Gancyclovir 5 mg/Kg/12 hrs for 2-3 wks IV infusion. Oral preparation is also available.

A.B.:

- AIDS leads to infection with CMV, *H. zoster* or *H. simplex*.
- AIDS leads to blindness mostly due to CMV infection → retinitis.



Measles (Rubeola)

- Caused by Paramyxovirus by droplet infection.
- One attack → high degree of immunity.

IP: 10 days.

Clinical picture

Catarrhal stage

- **Day 1-2:** fever, running nose, red watery eye (conjunctival suffusion).
- **Day 2:** cough, photophobia, Koplik's spots which are small, grayish lesions surrounded by an erythematous base on the mucous membrane opposite the second molar tooth.

Exanthematous stage

- **Days 3-4:** Maculo-papular rash (initially on the face then the rest of the body).
- **Day 6-7:** fever settles and rash ↓↓.

Complications

- Effects of virus: stomatitis, keratitis, pneumonia.
- Secondary bacterial infection: OM, bronchopneumonia-conjunctivitis.
- Neurological: encephalitis – sclerosing panencephalitis.

Treatment

- Isolation for 10 days from the appearance of rash.
- Antibiotic for bacterial infection.
- Active immunization, live attenuated with mumps & rubella (MMR).
- Passive immunization (human gamma globulins) for debilitated children.

Mumps

- It is spread by droplet infection.

IP: 18 days.

C/P & Complications (disease of school aged children & young adults).

- Fever – headache – trismus with tender enlarged parotid gland with elevation of the ear lobule.
- Orchitis unilateral and bilateral occurs in patients who develop mumps after puberty. Bilateral testicular involvement results in sterility in only a small percentage of patients.
- Pancreatitis.
- Meningitis.
- Encephalomyelitis.

Investigations

- The virus can be isolated from CSF or saliva.
- Serological tests e.g. complement fixation test.

Treatment

- Symptomatic TTT, with Orchitis give prednisolone 40 mg/d for 4 days.

Prevention

Mumps vaccine at 15 month with measles and rubella.



Rubella (German measles)

Caused by Togavirus through droplet infection, One attack → high degree of immunity.

IP: 18 days.

Risk of congenital abnormalities: (congenital rubella syndrome)

- It affects the fetuses of up to 80% of all women who contract the infection during the 1st trimester of pregnancy. The incidence diminishes to < 5% in the second trimester and almost no ill-effects in the 3rd trimester.
- Congenital rubella syndrome is characterized by VSD, PDA, cataract, deafness and mental retardation.

Clinical Picture

- Fever, rash (pink macules behind the ears and on the forehead, rash spread to trunk then to limbs).
- Tender enlarged suboccipital lymph nodes.
- Complications are encephalomyelitis, thrombocytopenia and polyarthritis.

Treatment

- If infection occurred during the first 16 wks of pregnancy termination is recommended.
- MMR vaccine for all children at age of 15 months. A second dose of rubella vaccine alone is given to girls aged 11-13 years.
- Women of childbearing age who are sero(-ve) should be vaccinated provided that they are not pregnant and are willing to avoid pregnancy for 12 wks after vaccination.

A.B.: Rubella & Measles & Mumps diagnosed by ELISA to detect Ab

IgM → recent infection.

IgG → Old infection.

Rubella also diagnosed by hemagglutination inhibition test after about 10 days from onset of the disease. It is diagnosed by very high or rising titre.

Rift valley fever

- It is an acute febrile illness of sheep, goats and camels.
- The vector is culex pipiens.
- I.P 3-6 days.
- The patient has fever lasts 2-4 days followed by a remission and a second febrile episode.
- Complications include retinopathy, meningoencephalitis, hepatic necrosis and haemorrhagic disorders. Mortality is about 50%.

Treatment is supportive.



D.D. of sore throat

(The commonest cause is viral infection)

1. Acute follicular tonsillitis:

- Flushing, high fever & follicles of pus.
- Throat swab is diagnostic (caused by streptococci).
- **Treatment:** penicillins.

2. Diphtheria: see before.

3. Ludwig's angina:

Cellulitis of the floor of mouth due to infection with microaerophilic streptococci.

4. Viral sore throat:

- Caused by adenovirus.
- Mild fever, malaise, anorexia, cough, rhinitis, conjunctivitis, laryngitis & hoarseness of voice.

5. Vincent's angina:

- Caused by *Borrelia vincenti* & *Bacillus fusiformis*.
- Occurs in debilitated children or on top of pyogenic infection.
- Ulceration & inflammation of oropharyngeal mucosa with purulent exudate → foul breath (**Halitosis**).
- **Diagnosis:** Gram stained smears showing gram (-ve) Spirochaetes & fusiform bacilli.
- Penicillin is the drug of choice.

6. Epiglottitis.....

Caused by H. influenza, stridor in absence of much hoarseness. Avoid using a tongue depressor or any instrument.

7. Candidiasis:

Common in:

- Patients under steroid or antibiotic therapy.
- Diabetics or AIDS patients.

Manifested by white cheesy exudate on the buccal mucosa & pharynx, on scrapping → raw bleeding surface.

Diagnosis is confirmed by microscopic examination.

8. Acute lymphoblastic leukemia.

9. IMN (EBV) see before.

10. Other leucopenic conditions: as agranulocytosis, aplastic anemia.

II. Herpangia:

- Caused by Coxsackie virus.
- There is a vesicular eruption of the fauces, palate and uvula.

12. Glossopharyngeal neuralgia:

- Pain in the throat & tonsillar fossa precipitated by swallowing (pharyngeal spasm).
- No physical signs.
- It is treated by tegretol & phenytoin.



FMF

Familial Mediterranean Fever is inherited as an autosomal recessive disease. The gene has been localized to chromosome 16, it produces a chemotactic factor inactivator. Failure to produce this factor leads to FMF attacks.

Clinical Picture

Attacks of fever, serositis e.g. peritonitis or pleurisy leading to abdominal pain or chest pain, arthritis, the typical acute attack lasts for 12-72 hours, but the arthritis up to one week, late it may be complicated by renal amyloidosis.

Investigation:

- During attack ESR ↑, ↑ CRP, ↑ fibrinogen and ↑ Amyloid A.
- X ray chest showing Pleural effusion in some cases.
- Renal biopsy may show amyloidosis (in long durated cases).

Treatment:

Regularly with colchicines 1-2 mg/d can suppress the acute attack and prevent development of renal amyloidosis.

Fever of undetermined origin (FUO)

Pyrexia of unknown origin (PUO)

Definition:

It is a condition in which fever is the dominant feature of patient's illness & its cause is unknown. It is a major diagnostic problem.

Criteria:

- Fever 38° C or more for at least 3 weeks (either intermittent or continuous).
- Diagnosis cannot be made in spite of doing all the following investigations.
 - Urine & stool examination.
 - Chest X-ray.
 - Blood picture.
 - Abdominal sonar.

Causes:

1. Infections: (40-50%)

- | | |
|--|----------------------------------|
| a. Mal-treated typhoid. | b. Chronic salmonellosis. |
| c. Tuberculosis. | d. Infective endocarditis (IEC). |
| e. Amoebic liver abscess. | f. Brucellosis. |
| g. Pyogenic abscess (pelvic or suphrenic). | |
| h. EBV, CMV infection. | |
| i. Septic arthritis in prothetic joint. | |



2. Neoplasms: (20%)

- | | |
|----------------------|----------------------------|
| a. Lymphoma. | d. Renal cell carcinoma. |
| b. Leukemia. | e. Bronchogenic carcinoma. |
| c. Multiple myeloma. | |

3. Connective tissue diseases: (10 %)

- | | |
|---------------------|--------------------------|
| a. S.L.E. | c. Rheumatoid arthritis. |
| b. Rheumatic fever. | d. Vasculitis. |

4. Miscellaneous: (10%)

- | | |
|---|--------------------|
| a. Chronic liver disease. | b. Thyrotoxicosis. |
| c. Hemolytic blood diseases. | d. Sarcoidosis. |
| e. F.M.F. | |
| f. Drug fever e.g. penicillins. There is usually rash, arthralgia & eosinophilia. | |

5. Factitious: (1-5%)

- Switching thermometers.
- Injection of pyogenic material e.g. milk.
- Taking hot drinks before temperature recording.

6. Undiagnosed: (5 %)

- The cases recover spontaneously or with antibiotics or anti-inflammatory drugs, or the fever remains recurrent and can be suppressed by steroids.

Diagnosis of FUO:

1. History: leukemia, TB, IEC.....

2. Physical examination:

Skin lesions, enlarged lymph nodes, heart murmur, abdominal masses, liver, spleen, pelvic organs in females & testis in males.....

3. Laboratory tests:

1. Complete blood picture & ESR for leukemia and infections.
2. Liver enzymes for hepatitis.
3. ELISA for CMV Ab and other viral infections.
4. Antinuclear Abs, anti-DNA, complement for SLE, Rheumatoid factor.
5. Blood culture for aerobes & anaerobes for infective endocarditis, typhoid.
6. Tuberculin test.
7. Brucella agglutination test.
8. Widal test.
9. Paul Bunnell test.

4. Imaging techniques:

- a. Chest X-ray (to be repeated) for TB.
- b. Pelviabdominal U.S. (to be repeated) for suphrenic, pelvic or liver abscess.
- c. C.T. scan pelviabdominal & chest.

5. Radionuclide scanning: Gallium or Tc, labeled leucocytes can localize an abscess.



6. Biopsies:

- a. Bone marrow for leukemia.
- b. Liver for chronic hepatitis.
- c. Lymph nodes for lymphoma, TB.
- d. Other tissues as the lung for sarcoidosis.

7. Laparoscopy:

May be required to confirm a gynaecological cause e.g. pelvic inflammatory disease (PID) or T.B peritonitis.

8. Therapeutic trials:

- Anti TB drugs e.g. INH and ethambutol.
- Anti-rheumatic drugs.
- Metronidazole for amoebic liver abscess.
- Chloroquine in suspected malarial infection.

Important definitions

- Fever is an elevation of body temperature above the normal circadian variation as a result of a change in the thermoregulatory center located in the anterior hypothalamus.
- The normal body temperature is 36.8 ± 0.4 °C.
- The maximum normal oral temperature at 6 A.M is 37.2 and at 4 P.M is 37.7.
- Using the above criteria, an A.M temperature > 37.2 or a P.M temperature > 37.7 would define a fever.

Patterns of fever:

- **Sustained:** persistent elevation of body temperature with minimal variation. It may be noticed in typhoid fever!?
- **Intermittent:** when there is an exaggeration of the normal circadian rhythm, when this variation is extremely large the fever is termed hectic fever this is common due to systemic infection or abscess elsewhere. When hectic fever occurs daily it is called quotidian.
- **Relapsing:** febrile episodes are separated by intervals of normal temperature. When paroxysms occur on the first and third days, the fever is called tertian e.g. p. vivax. Quartan fever means paroxysms occur on the first and fourth day e.g. p. malariae.
- **Remittent:** the temperature falls each day but not to normal level e.g. in T.B, viral diseases and many bacterial infections.

N.B.: Pel-Ebstein fever

Fever lasting 3 to 10 days followed by afebrile periods of 3-10 days, is classic for Hodgkin's disease and other lymphomas.

Mechanism of fever

Substances that cause fever are called pyogens and may be either exogenous or endogenous.

1. **Exogenous pyrogens** e.g. microorganisms and their products or toxins e.g. (endotoxin).
2. **Endogenous pyrogens** are produced by host cells e.g. monocytes/macrophages e.g. (IL1 and TNF).

Sequences of events required for the induction of fever:

Exogenous pyrogen e.g. bacteria or virus → + Macrophages → release of IL1 & TNF → to heat regulating centre in hypothalamus → ↑ PGE2 → ↑ thermoregulatory set point → ↑ heat production & ↑ heat conservation → fever.

Hyperthermia

It is an elevation of core temperature without elevation of the hypothalamic set point due to inadequate heat dissipation.

Causes:

1. Malignant hyperthermia due to halothane (anesthetic).
2. Neuroleptic malignant syndrome due to phenothiazines therapy.
3. Status epileptics.
4. Heat stroke.
5. Pontine haemorrhage.
6. Thyrotoxic crises.

Hypothermia

It is a central or core temperature of 35 °C or lower (rectal temperature).

Causes:

1. Myxedema coma.
2. Hypoglycemia.
3. Adrenal hypofunction.
4. Hypopituitarism.
5. Alcohol (↑ heat loss by peripheral vasodilatation and inhibition of shivering).
6. Prolonged exposure to cold.

Differential diagnosis of fevers

Fever with generalized lymphadenopathy:

i. Infective causes:

a. Bacteria:

- | | |
|-----------------|------------------|
| 1. Brucellosis. | 3. Secondary \$. |
| 2. TB. | |

b. Viral:

- | | |
|---------|---------|
| 1. IMN. | 3. CMV. |
| 2. HIV | |

c. Parasitic:

- | | |
|-------------------|-------------------|
| 1. Leishmaniasis. | 2. Toxoplasmosis. |
|-------------------|-------------------|

ii. Blood diseases:

- | | |
|----------------------------------|------------------------|
| 1. Acute lymphoblastic leukemia. | 3. Hodgkin's lymphoma. |
| 2. Chronic lymphocytic leukemia. | 4. Lymphosarcoma. |

iii. Miscellaneous:

- | | |
|---------------------|-----------------------------|
| 1. Still's disease. | 3. Sarcoidosis. |
| 2. Felty's disease. | 4. Drugs e.g. (hydantoins). |

N.B.:

Fever with localized lymphadenopathy e.g. Diphtheria, Anthrax and Vincent's angina.

Fever + Mediastinal L.N enlargement present in cases of sarcoidosis, T.B and lymphomas.

Febrile coma:

a. Infections

- | | |
|----------------------|---------------------|
| 1. Meningitis. | 4. Typhoid state. |
| 2. Encephalitis. | 5. Typhus. |
| 3. Cerebral malaria. | 6. Trypanosomiasis. |

b. Endocrinal diseases:

1. Thyrotoxic crisis.
2. Diabetic ketoacidosis with infection!?

c. Neurological causes:

- | | |
|----------------------|------------------------|
| 1. Pontine hge. | 3. Status epilepticus. |
| 2. Subarachnoid hge. | 4. Brain abscess. |

d. Physical causes as heat stroke.

e. Any commatosed patient with superadded infection.



Fever with splenomegaly:

i. Infective causes:

a. Bacteria:

- | | |
|----------------------------|-----------------|
| 1. Infective endocarditis. | 4. Brucellosis. |
| 2. Typhoid & paratyphoid. | 5. Miliary TB. |
| 3. Typhus. | 6. Secondary S. |

b. Viral:

- | | |
|---------|--------------|
| 1. IMN. | 2. HIV, CMV. |
|---------|--------------|

c. Parasitic:

- | | |
|----------------|-------------------|
| 1. Bilharzial. | 3. Kala azar. |
| 2. Malaria. | 4. Toxoplasmosis. |

ii. Blood diseases:

- | | |
|-----------------------|---------------|
| 1. Leukemias. | 3. Lymphomas. |
| 2. Hemolytic anemias. | |

iii. Miscellaneous:

- | | |
|---------------------|-----------------|
| 1. Still's disease. | 3. S.L.E. |
| 2. Felty's disease. | 4. Sarcoidosis. |

Fever with jaundice:

a. Hepatocellular jaundice:

- | | |
|---------------------|------------------|
| 1. Viral hepatitis. | 4. Yellow fever. |
| 2. Drug hepatitis. | 5. Septicemia. |
| 3. IMV. | 6. Cirrhosis. |

b. Obstructive jaundice:

1. Calcular cholecystitis + stone in CBD.
2. Liver secondaries.
3. Charcot's fever (ascending cholangitis).
4. Cancer head pancrease.

c. Hemolytic jaundice:

Any hemolytic attack is usually accompanied with fever e.g.:

1. Malaria (black water fever).
2. Aquired or congenital hemolytic anemia.

Fever with sore throat: (see sore throat)

Fever with epistaxis:

- | | |
|-------------------|--------------------|
| - Typhoid fever. | - Rheumatic fever. |
| - Acute leukemia. | - Lymphoma. |
| - Vasculitis. | |

Fever with pallor:

- | | |
|---------------------------|-------------------------------------|
| - Infective endocarditis. | - Malaria. |
| - Haemolytic crises. | - Malignancies e.g. Acute leukemia. |



Fever with skin rash:

1. Measles.
2. German measles.
3. Scarlet fever.
4. Chicken pox.
5. Typhoid.
6. Glandular fever.
7. Typhus.
8. Rheumatic fever.
9. Infective endocarditis.
10. Cerebro-spinal meningitis.

Fever with rigors or chills:

1. Acute pyelonephritis.
2. Malaria
3. Amoebic hepatitis.
4. Infective endocarditis.
5. Charcot's fever
(Ascending cholangitis).
6. Abscess elsewhere.
7. Septicemia and pyaemia.
8. Hemolytic crisis.
9. Brucellosis.
10. Rickettsial diseases.

N.B.

- Any fever with sudden onset is accompanied with rigors in the beginning as in lobar pneumonia, influenza, tonsillitis.
- Chills (sensation of cold occurring in most fevers).
- Rigors (chills + shivering with teeth chattering)
- Sweats occur with activation of heat loss mechanisms either due to use of antipyretics or to elimination of the febrile stimulus.

Fever with relative bradycardia:

i. Fevers without CNS involvement:

1. Influenza.
2. Typhoid fever.
3. Infective hepatitis.
4. Mumps.
5. Primary atypical pneumonia.

ii. Lesions of the CNS, with rapid increase in the ICT.:

1. Cerebro-spinal fever.
2. TB meningitis.
3. Brain abscess.
4. Pontine hge.

Immunology

The immune system protects against microbial infection, foreign substances and possibly tumors, but occasionally the immune response may damage normal host tissues. It is dependent upon two types of immune responses:

I- Non-specific immune response or (innate immunity) or natural resistance.

It is inborn with every one. It is the first line of defense. It consists of the rapidly acting host defence mechanisms and includes the following:

A. Physical or chemical barriers.

- Skin and mucous membranes.
- Gastric acid lysozymes.

B. Mechanical removal

- Sneezing, coughing.
- Secretions and urine (washing).
- Ciliary escalator of respiratory mucosa.

C. Colonization resistance

- Presence of normal flora in skin and gut preventing colonization by pathogenic organisms.

D. Nonspecific components.

- Phagocytes.
- Complement.
- Natural killer cells.
- Interferons.

II- Specific immune response or acquired or adaptive immunity.

In which antigens which overcome the innate nonspecific mechanisms of resistance will face the host's second line of defense.

Acquired immune response depends on humoral & cell mediated immunity. There is cooperation between the cells involved in both responses.

A. Humoral immunity:

In which antigen stimulates B lymphocytes, which proliferate into antibody forming cells (plasma cells) → Abs that react specifically with Ag.

B. Cell mediated immunity (CMI)

In which Ag sensitizes T lymphocytes, which are responsible for cell mediated immune responses. This initiated by Ags e.g. intracellular microorganism, tumors, transplanted tissues.

NOTE: Another form of immune responses called **immune tolerance** i.e. a state of immune paralysis towards a specific Ag. Example is the natural tolerance towards self Ags.

Tissues and Components of the Immune System

(Lymphoid tissues or organs, cells and biologically active substances).

The Immune system includes cellular and molecular components derived from the central and peripheral lymphoid tissues or organs. So, the immune system consists of the following:

1. Central lymphoid organs:

- Consist of bone marrow and thymus.
- They are the location of maturation of lymphoid cells.

2. Peripheral lymphoid organs:

- Consists of spleen, lymph nodes, tonsils, peyer's patches and appendix.
- They are the location of reactivity of lymphoid cells.

3. Cells of the immune system:

- Natural killer cells.
- Granulocytes.
- Monocytes and macrophages.
- Eosinophils.
- Lymphocytes (T & B).

4. Molecules of the immune system:

- Cytokines.
- Complement.
- Antibodies.

Lymphoid System

(central and peripheral lymphoid organs)

- All lymphocytes originate from the bone marrow and are programmed to carry out specific functions by certain lymphoid organs.
- T & β cells develop within the primary lymphoid tissues (thymus for T cells & bone marrow for β cells) and then circulate to the secondary lymphoid tissues (lymph nodes, spleen, tonsils and mucosa associated lymphoid tissue).

Natural killer cells (NK)

They are non B non T lymphocytes. They lack all types of receptors. They have an important non specific cytotoxic action against tumor cells, tissues, bacteria, and fungi. They involved in non specific immunity.



Phagocytic cells

Polymorphs (microphage)

Mononuclear phagocytic cells (macrophages)

In blood they are called monocytes, in tissues they are called (macrophages). They are involved in non specific immunity.

Macrophages:

Origin: Derived from BM precursors, which differentiates to blood monocytes which settle in tissues as mononuclear phagocytes.

Function:

1. Secretion of: IL1 → activates lymphocytes.
Tumor necrosing factor (TNF).
2. Acute phase response: to infection or injury through IL 1,6 & TNF.
3. Regulation of haemopoiesis.
4. Regulation of haemostasis: through secretion of thromboplastin.
5. Lymphocyte activation.
6. Killing of microorganisms.
7. Killing of tumor cells.
8. Tissue repair & remodeling.
9. Phagocytosis of immune complexes.

A.B: **Tissue macrophages:** Macrophages present in some organs, Includes:

1. Lungs: alveolar macrophages.
2. Liver: Von Kuffer cells.
3. Kidney: Mesangial cells.
4. Brain: Microglial cells.
5. Spleen: Litroral cells.
6. Skin: Langerhans cells.

Eosinophils

- They appear to be act selectively for fighting parasitic infections particularly nematode.
- Also they participate in type I hypersensitivity they secrete the followings:
 - Major basic protein → damage helminthes.
 - Eosinophil neurotoxin against parasites.
 - Eosinophil peroxidase kills bacteria, helminthes and tumor cells.



Lymphocytes

T Lymphocyte

Origin: derived from stem cells in BM & they mature in thymus.

Classes: proliferate & differentiate into:

- *T-helper/inducer with CD4 protein on their surface* → stimulate β lymphocytes and mediate delayed type of hypersensitivity by the cytokines they release e.g. tuberculin test.
- *T-suppressor/cytotoxic with CD8 protein on their surface.*
They suppress B lymphocytes and have the ability to kill other cells by apoptosis (programmed cell death).

B lymphocytes:

Origin: derived from stem cells in BM & complete maturation in BM.

Proliferate & differentiate into plasma cells.

Plasma cells → immunoglobulins (See later).

Cytokines

Def: soluble factors, which produce lymphocytes mediated effect.

Some are called interleukines & interferons.

Important cytokines & their sources:

α Interferon (INF):	Monocytes & macrophages.
β Interferon (INF):	Fibroblasts.
γ Interferon	T-lymphocytes.
Interleukine I:	Macrophages.
Interleukine II, III, IV, V:	T cells.
Interleukine VI:	T cells.
TNF:	Macrophages & T cells.

Some function:

- **Interleukin I, II** → T lymphocyte expansion.
- **Interleukin III** → haemopoetic cell expansion.
- **Interleukin IV, V, VI** → B cell expansion.
- **INF** → promotes intra cellular killing & ↓ viral replication.
- **TNF** → toxicity to tumor cells, also known as cachectin. It causes fever, weight loss, acute phase reaction (Associated with infection & tumor formation).



Complement

The complement system is an amplifying cascade similar to those responsible for blood clotting.

Classic pathway

- It is initiated by complement fixing antibody e.g. IgM, IgG (immune complex).
- It becomes activated with the following sequence $C_1, C_4, C_2, C_3 \rightarrow C_3$ B n followed by activation of C_5, C_6, C_7, C_8 and finally $C_9 \rightarrow$ cell lysis..

Alternative pathway

- It is initiated by bacteria or chemical stimuli or tumor cells and by aggregate Igs e.g. IgA, IgG.
- There is direct conversion of C_3 into C_3B , then the same as above.

Other biologic activities of complement

- Chemotaxis.
- Opsonization.
- $\uparrow$ vascular permeability.
- Platelet aggregation.

Immunoglobulins

- They are glycoprotein in nature; secreted by plasma cells.
- Composed of 2 types of polypeptide chains: heavy & light.
- On electrophoresis ; immunoglobulins are found in the gamma fraction.
- Fab region provides combining sites for Ag.
- Fc receptor: $\rightarrow$ transmission of IgG across the placenta.
 $\rightarrow$ attachment of IgE to mast cells.
 $\rightarrow$ Complement fixation.

IgG:

- Most abundant Ig in body fluids (75 % of total).
- Equally distributed in different fluid compartments (low MW).
- Important in defence against diffusing toxins & spreading microorganisms.
- Predominant Ig in 2ry immune response.
- Effective opsonin $\rightarrow$ promotes phagocytosis.
- Activates complement.
- Only Ig which can cross the placenta to the fetus $\rightarrow$ passive natural immunity for 3-6 months.



IgM:

- Essentially limited to blood stream preventing occurrence of septicaemia.
- Largest Ig with a pentameric structure, also it activates complement.
- Earliest response to antigenic stimulation (1st immune response)
- Its presence indicates recent infection.
- Neonate have high incidence of gram -ve septicaemia due to very low IgM level.
- ↑↑ IgM in neonates is an indication of intrauterine infection.
- Examples of IgM antibodies (natural antibodies): ABO, Rh factor.

IgA:

- Present both in serum & seromucous secretions of:
 - Respiratory, GIT & genitourinary systems.
 - Sweat, tears, saliva & colostrum.
- Secretory IgA inhibits entry of pathogens (antiseptic paint of m.m. against viral, & bacterial infections i.e: coats m.m.) → ↑↑ incidence of respiratory tract infection in IgA deficiency.
- Can activate complement.
- Secretory IgA confers immunity to infection by enteric bacterial and viral pathogens.
- Prevents undue IgE rise.

IgE:

- Normally found in small quantities in serum.
- Has tendency to fix to mast cells & basophils.
- Increase in IgE indicates:
 - immediate hypersensitivity e.g. atopy.
 - Parasitic infection.

IgD:

- Normally found in small quantities in serum.
- Present mainly on the surface of immature B cell which may be responsible for their maturation.

Q. Indications of Igs in medicine?

1. Prophylaxis of certain viral disease e.g. HAV, HBV.
2. Prophylaxis & therapy of: diphtheria, tetanus & gas gangrene.
3. Replacement therapy in 1st or 2nd humoral immune defence.
4. Prevention of maternal sensitization during parturition in case of Rh incompatibility.
5. High dose IV of ISG as an immunosuppressant for prevention of graft rejection.
6. Treatment of I.T.P, M. gravis and G. Barre \$.

Immunopathological conditions

The function of our immune system is recognition and elimination of the foreign antigens. Abnormal immune response can occur in one of the following three immunopathological conditions:

1. An exaggerated immune response

This leading to more damage rather than prevention of harm, this is called hypersensitivity reactions (Immune injury reactions).

2. Failure of self-recognition

This leading to autoimmunity (autoimmune diseases) which are classified into:

Organ specific:

- Hashimoto' thyroiditis.
- Graves' disease.
- Addison's disease.
- Autoimmune haemolytic anemia.

Organ non specific

- SLE.
- Rheumatoid disease.

3. Failure to produce an adequate immune response

This means immune deficiency (see later).

Hypersensitivity Reactions (Immune Injury Reactions)

Definition: Hypersensitivity defined as tissue damage resulting from an exaggerated immune response (changed reactivity of a host to an agent on a second or subsequent occasion). We have 5 types:

Type I = Anaphylactic reaction (Immediate reaction):

- This is due to IgE antibodies.
- IgE fixes with its Fc to mast cells → degranulation of the mast cells.

with release of pharmacologically active products e.g. histamine, serotonin (causing bronchoconstriction and increased vascular permeability).

- Also there is release of neutrophil and eosinophil chemotactic factors (they induce inflammatory cell infiltration). Leukotriene and prostaglandins causing sustained bronchoconstriction and edema.

Hypersensitivity of this type includes the manifestations of familial atopic diseases; in which there is a strong familial predisposition to produce high levels of IGE (genetically predisposed individuals):



Diseases due to type I hypersensitivity include:

- Atopic eczema.
- Allergic rhinitis.
- Anaphylactic shock.
- Asthma (extrinsic).
- Food allergies.
- Urticaria and angioneurotic edema.

Diagnostic tests:

Skin prick tests leading to wheal within 5-10 minutes.

Treatment:

- Antigen avoidance – Antihistaminics.
- Corticosteroids (topical or systemic).
- Sodium cromoglycate.

C\P of anaphylactic shock:

1. History of Ag exposure, nausea, vomiting and diarrhea.
2. Shock.
3. Bronchospasm and laryngeal edema may occur.

TTT of anaphylactic shock:

- Adrenaline 1/1000, 0.5-1 ml I.M and repeat after 10-20 minutes if shock persists.
- Hydrocortisone IV 100-300 mg I.V.
- Antihistaminics e.g. chlorpheniramine 10 mg I.V..
- Aminophylline I.V. with bronchospasm.
- I.V fluids if hypotension persists and O₂ therapy or assisted ventilation if hypoxia is severe.

Type II = Cytotoxic reaction (Antibody Dependent):

- There are circulating antibodies (IgG or IgM) react with Ag (inside a cell or at its surface) + complement activation → damage of host tissue.
- This involves the death of cells bearing antibody attached to a surface antigen.
- The cells may be taken up by phagocytic cells or they may be lysed by complement.
- Cells bearing IgG may also be killed by killer Cells (antibody-dependent cell mediated cytotoxicity).
- Examples: Transfusion reactions, autoimmune hemolytic anemia, good pasture's syndrome, pernicious anemia and myasthenia gravis.
- Immunological diagnosis: Coomb's test.

Treatment:

- Plasmapheresis.
- Exchange transfusion.
- Immunosuppressives.

Type III = (Complex mediated hypersensitivity)

Pathogenesis: results from the effect of deposition of Ag-Ab complexes.

- The immune clearance of soluble Ag is achieved by:
 - Complexing with Ab mainly IgG, or IgM.
 - Elimination of immune complexes is usually by phagocytic cells.
- Failure of elimination leading to deposition of immune complexes in the wall of blood vessels and in the tissues with complement activation → cellular damage.
- Tissues liable to deposition of immune complexes: kidney → acute GN, lung → farmer lung, arteries → arteritis e.g. polyarteritis nodosa.

A.B.: The most important cause of immune complex disease is failure of soluble antigen clearance (**persistent antigenemia**).

Etiology of immune complex diseases i.e. persistent antigenemia:

Exogenous Ags	Endogenous Ags
1. Infection: - Bact.: infective endocarditis. - Protozoa: malaria. - Viruses: HBV, EBV, CMV. 2. Drugs: penicillin, sulfa, Quinine, insulin. 3. Vaccines: rabies, DPT.	1. Autoimmunity: IgG: rheumatoid disease. - Nucleic acids: SLE. 2. Tumors: lymphoma, renal carcinoma.

Types of type III reaction:

Arthus reaction	Serum sickness
Local type <u>Cause:</u> ID injection of Ag in a sensitized person (with high Ab titre). <u>Example:</u> local injection of antirabies vaccine or Antibiotics. <u>C/P:</u> - Local: edema, with erythema. - Features of acute inflammation within 6-24 hours.	Systemic type <u>Cause:</u> Ag excess → + IgG → circulating immune complex. <u>Example:</u> Large doses of horse serum or penicillins. <u>C/P:</u> - Fever, rash, LN++, arthralgia, peripheral neuritis, urticaria, GN, (onset 10 days after initial exposure to the antigen). - The disease is usually self limiting.

A.B.:

- When Ab levels are high, the Ag is precipitated near the site of entry e.g. farmer's lung.
- When the Ag is in excess → complexes at sites of increased vascular permeability e.g. the glomerular blood vessels (GN) or P.A.N.



Other conditions with serum sickness like illness:

- GN.
- SLE.
- Rheumatoid D.
- Vasculitis.
- Farmer's lung

Diagnosis of immune complex disease:

1. Measurement of:

- Circulating immune complexes (CIC).
- Serum Igs.
- Complement.

2. Detection of:

- Rh factor.
- Anti-DNA as in SLE.

Treatment of type iii (immune complex reaction)

- Corticosteroid.
- Plasmapheresis.
- Immunosuppressives.

Type IV: Cell Mediated (Delayed Type)

This is based upon the interaction of Ag with activated T cells → tissue damage resulting from cell mediated immune reactions, examples are:

Contact dermatitis

It is a local eczema occurs maximal at 48 hours, caused by chemicals. It is epidermal and the Ag is presented by the Langerhans cells.

Chronic infections

Activation of T lymphocytes by intracellular agents e.g. TB, leprosy, syphilis and many viral infections. The classic example of this reaction is tuberculin.

Other granulomatous diseases

e.g. Crohn's disease or sarcoidosis.

Diagnostic tests:

Skin test e.g. tuberculin test showing erythema and induration within 48-72 hours.

Treatment:

- Treatment of the cause.
- Corticosteroids.
- Immunosuppressives.

Type V: Stimulatory Hypersensitivity:

The antibody reacts with hormone receptors for example e.g. thyroid stimulating autoantibody in grave's disease (TSI).



Food allergy (food hypersensitivity) and food intolerance

Presentations

Acute hypersensitivity:

- Urticaria, vomiting or diarrhea after eating strawberries or shellfish anaphylactic shock may occur. This is mediated by IgE.

Eczema and asthma:

- This is common in children and treated by removal of eggs from diet.

Rhinitis and asthma:

- Mostly due to milk and chocolate in atopic persons.

Chronic urticaria:

- Treated mainly by diet exclusion.

Migraine:

- It may be occur following chocolate, cheese and alcohol (it is not a true allergic phenomenon).

Gluten sensitive enteropathy.

Other disorders:

- Histamine may be released by tomatoes.
- Milk induced diarrhea in alactasia.
- Fava-bean in G6PD deficiency
- Toxic chemicals in food (food additive).
- Tyramine in cheeses.

Management:

- Careful history.
- Skin prick testing.
- Diagnostic exclusion diet.
- Dietary challenge.
- Medications as antihistaminics, steroids and mast cell stabilizer may be needed.

Immunological Emergencies

- Immune injury reactions (see before) e.g.:**
 - 1- Anaphylactic reaction.
 - 2- Cytotoxic reaction.
 - 3- Immune complex.
- Infection in immunocompromized patients (see opportunistic infections).**
- Emergency immunization & Vaccination.**
- Immune mediated drug resistance.**
- Graft rejection.**
- Vaccination reactions.**



Emergency Immunization & Vaccination

Indications:

- 1- Medical staff wounded while handling infected material.
- 2- Pregnants & alcoholics in contact with viral hepatitis.
- 3- Infants < 6m in contact with measles.
- 4- Immunocompromised patients during epidemics or pandemics.
- 5- Immunocompromised children in contact with cases of measles.

Treatment and prophylaxis:

- 1- Anticipated prophylactic vaccination.
- 2- Immune serum globulins (non-specific Abs).
- 3- Hyperimmune globulins (contain specific Ab of the disease).

Immune Mediated Drug Resistance

Example: Insulin resistance; is the need of more than 200 units/d, in the absence of ketosis.

Causes:

<i>Non-Immunological:</i>	<i>Immunological:</i>
1- Obesity. 2- Ketosis, Infection. 3- Other endocrinopathies (cushing, acromegaly). 4- surgery.	1- Insulin receptor abnormality. 2- Insulin antibody.

Treatment:

- 1- Weight reduction, causal ttt e.g. infection, obesity or cushing \$.
- 3- Add steroids → ↓ insulin requirements (in cases of insulin antibody).
- 4- Shift from pork to beef or the reverse.
- 5- Use of human insulin.

Graft versus host reaction (GVHR) = Runt disease

Definition: After bone marrow transplantation there is a triad of:

- (1) cutaneous lesions (morbilliform rash, skin desquamation)
- (2) Gastroenteritis
- (3) Hepatitis.

Treatment:

- 1- Proper HLA matching.
- 2- Immunosuppressives.

Acute Graft rejection (see later)

Vaccination reaction



Autoimmunity

- Autoimmune disease occurs when the immune system fails to recognize the body's own tissues as self and mounts an attack on them.
- A defect in immunological tolerance may either occur spontaneously or may be induced by some exogenous factor e.g. viral infection, often in genetically predisposed individual.

Classification of autoimmune diseases

I- Organ specific

- Hashimoto's thyroiditis.
- Graves' disease.
- Good pasture's S.
- Primary biliary cirrhosis.
- Autoimmune addison's disease.
- Autoimmune chronic active hepatitis.
- Primary hypothyroidism.
- Pernicious anemia.
- Type I D.M.
- Myasthenia gravis.

II- Organ non specific

- Rheumatoid disease.
- Systemic sclerosis.
- Dermatomyositis.
- SLE.

Theories of autoimmunity

I- Aberrant immunity

- The cells of a target organ express MHC class 2 antigens on their surfaces this → + T helper cells. Viruses are implicated in the abnormal expression of MHC antigens.
- Loss of suppressor T cell control of the T helper cells.

2- Antigen recognition

- Release of sequestered antigens e.g. extravasation of sperm → sperm antibodies → sterility.
- Sharing antigen (cross sensitivity) e.g. rheumatic carditis.

3- Autoantibodies

Immunodeficiency

Congenital or primary Immunodeficiency:

I. B-cell defect = X-Linked hypogammaglobulinaemia (humoral immunodeficiency):

- Onset: 3-6 month of age (until disappearance of maternal IgG).
- Repeated pyogenic infection eg ASOM, pneumonia .
- Few problems with fungal or viral infections except enteroviruses.
- No or few β cells in blood, normal T cells function and number.
- Decrease of IgM, IgE, IgA and IgG.



2. T-cell defect = Di George \$, (Thymic & parathyroid aplasia)

- Infection with opportunistic organisms e.g.: candida, viral, pneumocystitis carinii.
- Tetany causes hypocalcaemia due to absence of parathyroid glands.
- Delayed hypersensitivity skin tests e.g. tuberculin test are -ve (**anergy**).
- The defect of this condition has been found on chromosome 22.

3. Stem cell defects = (severe combined immunodeficiency with B & T cell defects)

Presents in the first weeks of life by:

- Repeated pyogenic infections.
- Opportunistic infections.
- Absent tonsils. Absent thymic shadows.
- Failure to thrive.
- Severe lymphopenia (T & β cells).

A.B.: Ataxia telangiectasia and wiskott-aldrich syndrome (chronic suppurative otitis media + thrombocytopenia) are also considered as combined immunodeficiency.

4. Phagocytic deficiencies → granulomatous disease. e.g. chediak-Higashi \$, and hyper IgE syndrome.

5. Deficiencies of complement:

This leading to immune complex like or lupus like disorders.

Deficiency of complement inhibitor (C_1 inhibitor):

- Hereditary angioedema affecting the face and gut.
- Blood level of C_1 inhibitor are low.
- The disease can be treated with danazole as it increases C_1 inhibitor.

Acquired immunodeficiency:

- 1- Age: ↓ immunity in infancy and elderly. ↓ Self tolerance in elderly → autoimmunity.
- 2- Malnutrition leads to Abs defects, T-cell defects if severe.
- 3- DM → neutrophil dysfunction (migration and phagocytosis).
- 4- Infections: non-specific decrease of CMI e.g. AIDS, measles, \$, leprosy.
- 5- Neoplasms: eg. Leukaemia → neutrophil dysfunction, lymphoma and multiple myeloma → Ab deficiency (B cell defect).
- 6- Drugs: steroid → neutrophil dysfunction, myelosuppressive → neutropenia.
- 7- Loss of protective commensal gut flora due to use of broad spectrum Ab.
- 8- Post operative, G anesthesia → immunodeficiency for several days.
- 9- Postsplenectomy → Antibody deficiency (B cell defect).



Isolated Humoral Immunodeficiencies

I. IgA deficiency

Causes:

- 1- Genetic.
- 2- Drugs: phenytoin, sulfasalazine, penicillamine.
- 3- Viral: EBV, rubella.
- 4- Iatrogenic: splenectomy, B.M. transplantation.

Clinical Picture:

- 1- Usually asymptomatic.
- 2- Recurrent infections: e.g. respiratory tract and pyogenic infections.
- 3- Dysimmunity: atopy, allergy or autoimmune diseases.

Treatment: Replacement-plasma transfer.

2. IgM deficiency

This renders patients liable to blood borne infections such as meningococcal infections.

A.B.: Decrease of Immunoglobulin may lead to malabsorption syndrome due to *Giardia lamblia* infection and bacterial overgrowth of small intestine.

Opportunistic Infections

(Infections in immunocompromised patients)

These infections are caused by opportunistic pathogens or organisms i.e. organisms that taking the advantage of the opportunity of impaired host defence mechanisms.

Types of opportunistic infections:

I. Opportunistic infections in cases of non immunological defence defects include:

- Haemophilus influenza and pneumococci in smokers.
- Pseudomonas in cystic fibrosis.
- Gram negative infections in urinary tract obstruction.
- Candida and pathogenic E coli following elimination of gut flora after antibiotic therapy.
- Staphylococcal and candidal infections with indwelling venous catheters.



2. Opportunistic infections in cases of immunological defence defects include:

a) **Neutrophil defects** → infections with *Staph*, *E coli*, *Proteus*, *Klebsiella*, *Pseudomonas*, *Aspergillus*, *Candida* and *mucor mycosis*.

b) **Opsonin defects**

- This is due to antibody deficiencies, or defects of complement pathway and splenectomy leading to infection with capsulated organisms.
- These organisms can not be eliminated by neutrophils alone, as the capsule prevents phagocytosis unless opsonized by either antibody or complement.
- The capsulated organisms are *H. influenza*, *Meningi cocci* and *pneumococci*.

c) **Antibody deficiency** → infections with *mycoplasma*, *echovirus* & *campylobacter*.

d) **Complement pathway defects:**

- This leading to infection with *Meningococcus*.
- Also disseminated gonococcal infection can occur.

e) **Cell mediated immunodeficiency**

- This affects the harmony between CD₄ T cells and macrophage leading to infections with intracellular pathogens e.g. *Mycobacterium tuberculosis*, *Atypical mycobacterium*, *Candida*, *Pneumocytosis carinii*, *Toxoplasma*, *Herpes simplex*, *Herpes zoster*, *CMV* and *Ebstein-bar virus*.

Lines of defense and clinical applications

First line of defense (physical or chemical barriers and mechanical removal):

1 - Skin:

- 1 Skin keratin: physical barrier.
- 2 Sebum: bacteriostatic.
- 3 Sweat: acidity.

2- Mucous membrane:

1- Physical	2- Chemical	3- Mechanical	4- Immunological
Continuity of mucous membrane.	1. Enzymes: lysosymes. 2. Acidity: GIT, urine.	1. Cough + muscular escalator. 2. Peristalsis of GIT.	1. IgA. 2. Bacterial flora.



Second line (cellular & humoral components):

A. Cellular components	B. Humoral components
1- Leucocytes especially neutrophils: <i>Function:</i> a- Aggregation & adherence. b- Diapedesis & migration. c- Chemotaxis. d- Phagocytosis.	1- Complement especially alternative way <i>Function:</i> a- ↑ Capillary permeability (C ₅ a). b- ↑ Chemotaxis (C ₅ a). c- Eliminate organism from blood stream.
2- Macrophages.	2- PG & leukotriens: ↑ Capillary permeability, ↑ chemotaxis.

Third line of defense (specific or adaptive immunity):

A- Cell mediated immunity

= T lymphocytes → direct killing + cytokines secretion.

B- Humoral immunity

= B cell-plasma system → Igs secretion (see before).

Clinical applications:

1st line: failure

Causes:

- 1- **Traumatic/pathological:** wounds, stones, IgA deficiency.
- 2- **Iatrogenic:** Invasive techniques, operation, antacids & cough suppressants.

Prophylaxis:

- 1- Dental hygiene + oral Nystatin if needed.
- 2- Avoid constipating agents.
- 3- Minimum hospital stay.

Treatment: Antibiotic + Causal ttt.

2nd line failure:

Causes:

- 1- **Cellular:** ↓ neutrophil.
↓ neutrophil function [adhesion (steroids), chemotaxis].
- 2- **Humoral:** ↓ Complement [congenital, consumptive (dialysis)].

Treatment:

- 1- Antibiotics: Parenteral, bactericidal, usual dose for prolonged time.
- 2- Plasma transfusion: contain Ig & complement.
- 3- Levamisole: ↑ macrophage function.



3rd line: failure

Causes:

See before (immunodeficiency).

Diagnosis:

1- Culture and sensitivity & direct films to diagnose the infection.

2- To diagnose immune system dysfunctions:

a. *Humoral immunity*: Immunoglobulins measurement.

b. *Cellular immunity*: lymphocytic count, tuberculin test.

Treatment:

1-For infection:

a- Antibacterial therapy.

b- Antifungal: oral mycostatin, ketoconazole.

c- Antiviral.

2- For Humoral immunity: plasma transfer, ISG (immunserum globulins).

3- For Cellular immunity: stop steroids, Cytokines therapy.

Immunomodulation (Immunotherapy)

I. Immunization:

- Active immunization gives protective immunity to many infectious diseases.
- Passive immunization i.e. administration of immunoglobulin (see before).

2. Interferon therapy and other cytokines:

i. Interferon:

Uses: HBV, HCV, CML, D.S., m. melanoma, kaposi sarcoma.

Mech: stimulates macrophages & NK cells, inhibits viral replication.

Side effects: flu like picture, myalgia, nausea, headache, thyroiditis.

ii. Thymic hormones.

iii. Interleukines.

Immunoglobulins, thymic hormones, thymic transplantation or interleukins therapy can be used as a treatment of immunodeficiency syndromes.

3- Immunopotentialiation with levamisol & BCG:

Levamisol:

Uses: SLE, rheumatoid arthritis, adjuvant in breast cancer.

Mech: ↑macrophage chemotaxis.

Side effects: flu like \$, nausea, dermatitis, metallic taste.

BCG: uses: anti neoplastic (malignant melanoma, lung cancer or bladder carcinoma).



4- Grafts:

a. B.M. transplant:

Indications:

- Aplastic anemia.
- Acute leukemia.
- Myelofibrosis

b. Thymus transplant.

5- Apheresis:

a. Plasmapheresis: removal of large plasma volume.

Indications: TTP, GB\$, ITP, Myasthenia gravis, Good pasture \$. Rapidly progressive G.N, malignant exophthalmos and hyperviscosity \$ e.g. Waldenstrom's disease.

b. Leucopheresis:

6- Treatment of hypersensitivity by:

- Hyposensitisation.
- Antihistamines.
- Sodium cromoglycate.
- Adrenaline and aminophylline.

7- Immunosuppression by medications:

1- Cytotoxic drugs.

2- Steroid therapy.

3- IV immune serum globulin (ISG) therapy:

It is used as an immunosuppressant (↓ Fc receptor of macrophages).

8- Monoclonal therapy

It is a recent method of immune therapy. Antibodies are produced by biotechnology. These antibodies used against tumor cell, leukemia cells, bacterial toxins and cytokines.

Major Histocompatibility Complex (MHC)

The MHC gene cluster is located on chromosome 6, it contains genes coding for the human leucocytic antigens (HLA). These Ags are found on many cells (not only leucocytes).

Value of determination of HLA typing:

- 1- Transplantation e.g.: heart, kidney.....
- 2- Some diseases are associated with certain HLA types e.g.:
 - a. Ankylosing spondylosis: B₂₇.
 - b. Psoriasis: B₁₃
 - c. IDDM: Dr₃, Dr₄..



Graft rejection after renal Transplantation as an example

1. Hyperacute rejection

- Due to preexisting antibodies, which bind to the endothelium where type II cytotoxic reaction occurs.
- This leads to thrombotic occlusion of the graft vasculature within minutes after vascular anastomosis.

2. Acute rejection

- It occurs within 10-90 days of transplantation.
- It is associated with vasculitis (Type III immune complex) and/or it is associated with delayed hypersensitivity reaction. The first type is called acute humoral rejection, the second type is called acute cellular rejection.

3. Chronic rejection:

- It occurs after months or years, it is a chronic delayed hypersensitivity reaction with fibrosis & sclerosis of the glomeruli (The process is irreversible).

AB: Prevention and TTT of graft rejection → see nephrology.

GVHR → see hematology.

AIDS: Acquired Immune Deficiency Syndrome

Def.: AIDS is the end stage manifestation of a long standing infection with a retrovirus (HIV).

The virus:

- 1- HIV1: Predominates in Central Africa, Asia, Europe and North America.
- 2- HIV2: Predominates in Western Africa.

Risk groups:

- 1- Homosexuals and heterosexuals.
- 2- IV drug abusers.
- 3- Hemophiles.
- 4- Blood transfusion recipients.

Transmission: Semen & blood via mucous membrane.

1- Blood born: blood transfusion, sharing needles, accidental, unsterile needles, and organ donations.

2- Sexual: Homosexual, heterosexual.

3- Vertical transmission from mother to child during delivery, also by breast feeding.

4- Dental procedures.



Incubation period: 4-6 weeks up to years. After 4-6 weeks the patient may present as group A, after months or years the patient may present as group B or C (see below).

Pathogenesis: (Immunological abnormalities)

Main targets of a retrovirus (HIV) are:

- 1- T4 (T-helper cells) lymphocytes decreased in number with abnormal function.
- 2- Abnormal function of monocytes & macrophage.
- 3- Abnormal function of β lymphocyte.

Clinical presentation

- Patients may present with IMN like + persistent generalized lymphadenopathy (presence of enlarged lymph nodes greater than 1 cm in diameter in two anatomically distinct sites for > 3 months).
- Or by HIV associated conditions e.g. fever, diarrhea, ITP, ...
- Or by frank AIDS with opportunist infections and neoplasms.

Classification of HIV associated conditions:

Group A:

Asymptomatic or persistent generalized lymphadenopathy or acute HIV infection (IMN like).

Group B:

HIV or AIDS related complex

- | | |
|--|--------------------------|
| - Fever. | - ITP. |
| - Weight loss. | - Oral candida. |
| - Diarrhea. | - Peripheral neuropathy. |
| - LN enlargement. | |
| - <i>H. zoster</i> in more than one dermatome. | |

Group C:

Clinical conditions meeting with definition of AIDS.

I- HIV associated infections:

- Disseminated CMV, CMV retinitis.
- Disseminated candidiasis, *Herpes virus*.
- *Mycobacterium avium*, tuberculosis.
- Extraintestinal strongyloidiasis.
- *Pneumocystis carinii* (commonest opportunistic infection in AIDS).
- Toxoplasmosis of brain.

II- HIV associated malignancy:

- | | |
|---------------------|---------------------------|
| - Lymphoma. | - Non Hodgkin's lymphoma. |
| - Kaposi's sarcoma. | - Primary brain lymphoma. |



Effects of HIV infection on different systems

1- Skin

- Seborrhea.
- Secondary \$.
- Fungal infections.
- Drug eruption.
- Folliculitis, cellulitis, impetigo.
- Herpes simplex.
- Herpes zoster.
- Kaposi's sarcoma.

2- GIT

- **Mouth:** candidiasis, Angular stomatitis, Aphthous ulcers, Herpes, Kaposi sarcoma.
- **Oesophagus:**
 - Esophagitis by candida, herpes and CMV.
 - Kaposi sarcoma.
- **Stomach:** Kaposi, CMV, Mallory-Weiss and variceal bleeding due to associated hepatitis B, C and ethanol intake.
- **Small bowel diseases:**
 - Salmonella.
 - Giardia.
 - CMV.
 - Kaposi sarcoma.
 - Strongyloides..
- **Colorectal:** CMV colitis - tenesmus

3- Hepatobiliary

Hepatitis B, C, CMV with hepatomegaly.

4- Respiratory disease

- *Pneumocystis carinii*.
- CMV.
- Candida, Aspergillus.
- Interstitial pneumonitis.
- *M. avium* & tuberculosis.
- Pneumonia.
- Kaposi, sarcoma.
- Lymphoma.

Main features of tuberculosis in HIV infection

- Most cases due to reactivation.
- Extrapulmonary TB is common.
- TB may accelerate HIV disease.
- Tuberculin test is -ve (**anergy**).
- 6-9 months therapy is recommended but INH prophylaxis should continue for life to prevent relapse.

5- Nervous system

- HIV (Direct infection): Encephalitis, meningitis, dementia, peripheral neuropathy, and myelopathy.
- Other infections.
 - Toxoplasma, Brain abscess.
 - CMV → encephalitis or retinitis.
 - TB → meningitis.
 - Herpes zoster → meningitis.
- Tumors as primary lymphoma.



6- Blood

ITP, lymphoma. Anemia due to BM infiltration by TB or lymphoma, blood loss from Kaposi sarcoma or B₁₂ ↓ due to malabsorption on top of intestinal infections.

7- Renal

- HIV nephropathy.
- Drug nephropathy (nephrotoxicity).

8- Heart: Myocarditis, pericardial effusion.

9- Endocrine: CMV adrenalitis.

10- Psychiatric problems

A positive HIV test result in a variety of reactions e.g. anger, guilt, anxiety with panic attacks and depression.

Investigations of HIV infection

- 1- HIV Ab, PCR.
- 2- Anemia, leukopenia and thrombocytopenia.
- 3- Low number of T-helper cells < 400/mm³, patients with counts <200 at a very high risk.
- 4- Helper / suppressor T-cell ratio <1.
- 5- ↑ serum immunoglobulin level (abnormal function of B lymphocytes).
- 6- ↑ ESR.
- 7- Cutaneous anergy.

Treatment of HIV infections:

- 1- Prophylaxis - screening - counselling - condoms - society education.
- 2- AZT ® zidovudine: 500-1000 mg/D orally. Lamivudine can be used also.
- 3- Immune-therapy: interleukins, interferons, isoprinosine, lymphocyte transfusion.
- 4- Opportunistic infection:
 - Pneumocystis carinii ttt by sutrim infusion.
 - H.S. and H.Z. ttt by acyclovir.
 - Candidiasis ttt by amphoterecin B.
- 5- Chemotherapy + irradiation for lymphoma.

Post exposure prophylaxis

Combination of Zidovudine and Lamivudine for 4-6 wks.

- It is recommended following needle stick injuries or other parenteral exposure with known HIV infected material
- It has been shown to reduce but not remove the risk of infection.

A.B.:

Zidovudine is nucleoside-analogue reverse transcriptase inhibitor (NRTI).

Side effects

- | | |
|-------------|------------------|
| - Nausea. | - Headache. |
| - Insomnia. | - BM depression. |

Other antiretroviral (NRTI)

- | | |
|---------------|---------------|
| - Lamivudine. | - Didanosine. |
|---------------|---------------|



GENETICS

I. Single Gene Disorders (inheritance is according to Mendelian laws)

1- Autosomal Dominant Inheritance

- Adult polycystic kidney disease.
- Huntington's disease.
- Familial hypercholesterolaemia.
- Congenital spherocytosis.
- Polyposis coli.
- Neurofibromatosis.

2- Autosomal Recessive inheritance

- Cystic fibrosis.
- Hemochromatosis.
- Sickle cell anemia.
- β thalassemia.
- α 1 antitrypsin deficiency.
- Wilson's disease.

3- X Linked recessive

- Duchenne muscular dystrophy.
- Hemophilia A.
- Becker muscular dystrophy.
- Hemophilia B.

4- X Linked Dominant: Vitamin D resistant rickets.

A.B:

X Linked recessive inheritance

The affected boy has affected maternal uncle and his mother is carrier.

X Linked dominant inheritance

- If the mother is affected, the disease will be transmitted to either sex.
- If the father is affected, the disease will be transmitted to the daughters only.
- So all X linked inheritance shows the absence of male to male transmission.

II. Chromosomal Disorders

1- Autosomal:

E.g. Down syndrome.

- Flat profile.
- Upwards slanting eye.
- Congenital heart D.
- Small nose.
- Simian crease.
- Floppiness in neonate

2- Sex:

Klinefelter (47,XXY)

- Small testes.
- Infertility.
- Gynecomastia.
- Poor 2ry sex characters.

Turner (45,X)

- Short stature.
- Primary amenorrhea.
- Coarctation of aorta.
- Webbed neck.
- Poor 2ry sex characters.



III. Multifactorial disorders (polygenic)

- These disorders are caused by unknown multiple genes and environmental factors.
- There are familial aggregations i.e. more frequent in members of a family than in the general population.
- **Examples:** Intelligence, height, weight and blood pressure, asthma, C. Hr. D.

Management and prevention of genetic disorders

1. Genetic counseling

2. Prenatal diagnosis and screening

3. Gene therapy:

- Attempts to treat genetic disorders by introduction of normal genes into tissues expressing defective ones.
- It is important to find a delivery systems to introduce DNA into a mammalian cell
- ***Examples of diseases suitable for gene therapy***
 - Cystic fibrosis
 - Familial hypercholesterolaemia
 - Thalassemia, Hemophilia
 - Muscle Dystrophy e.g. (Duchenne)

Polymerase Chain Reaction (PCR)

- Minute amounts of DNA can be amplified over a million times within a few hours using this technique.
- The exact DNA sequence to be amplified needs to be known because the DNA is amplified between two short single standard DNA fragments (primers), which are complementary to the sequence at each end of the DNA of interest.
- This reaction can be used in diagnosis of infections, malignancy and other diseases.

GERIATRIC MEDICINE

I- Physiological effects of aging

- Diffuse hair loss.
- Reduced smell.
- Presbyopia, lens opacity.
- Cervical spondylosis.
- Loss of lung compliance.
- Reduced GFR & tubular function.
- Loss of skin elasticity.
- Osteoporosis.
- Osteoarthritis.
- Reduced neurone capacity.
- Reduced taste.
- Dilatation of aorta.
- Reduced Stroke volume.
- Systolic H, postural H.
- Impaired glucose tolerance.
- Constipation.
- Muscle wasting.
- Reduced number of sweat gland.
- Reduced position sense.
- Reduced hearing.

II- Disorders presenting with atypical features (e.g. confusion) in elderly Pts.

- MI or pulm. Embolism → confusion, blackout.
→ dyspnea.
→ palpitation without chest pain.
- Pneumonia → confusion with no fever.
- Peptic ulcer → anemia, GIT bleeding, without dyspepsia.
- UTI → confusion and urinary incontinence.
- Hyperthyroidism → apathy, weight loss, cardiac signs without anxiety.
- Hypothyroidism → lethargy.
- DM → asymptomatic until complications e.g. diabetic triopathy.
- Brain tumor → confusion without headache.

III- Giants of Geriatric Medicine

- These refer to four of the most common causes of incapacity in elderly patients referred to a geriatric unit.

1. Acute confusion (see above, investigation and treatment of the cause)

2. Urinary incontinence

- Due to cerebrovascular disease, Alzheimer's disease, prostatic obstruction.
- After menopause the atrophic changes in bladder and urethra are similar to the vaginal changes giving rise to frequency and urgency.
- Also faecal impaction may lead to pressure on the bladder leading to incontinence.
- Also diabetic autonomic neuropathy is an important cause.



Diagnosis

- History including the duration and timing of the incontinence, any associated urinary symptoms and drug treatment.
- Examination of the abdomen, nervous system, rectum and vagina is important.
- Culture of urine, pelvic sonar and urodynamics are important.

Treatment

- Toilet training e.g. regular emptying of bladder.
- Bladder relaxant e.g. oxybutinin.
- Oestrogen vaginal cream for atrophic vaginitis.

3. Immobility

Due to age changes in the neurological or musculoskeletal system.

Causes of immobility

- Stroke.
- Parkinsonism.
- Osteoarthritis.
- Osteoporosis.

Treatment

- Treatment of the cause.
- Rehabilitation.

4. Falls

Due to neurological, cardiovascular, musculoskeletal disease or drugs causing drowsiness, or postural hypotension.

Causes of falls in elderly patients

- **Neurological:**
 - Cerebrovascular disease.
 - Vertebrobasilar insufficiency.
 - Transient ischemic attacks.
 - Parkinsonism.
 - Visual impairment.
- **Locomotor:**
 - Osteoarthritis.
 - Muscle weakness.
 - Other arthropathies.
 - Cervical spondylosis.
- **Cardiovascular:**
 - A.S.
 - Sick sinus syndrome.
 - Adams-stokes attack.
 - Postural hypotension.
- **Drugs:**
 - Diuretics.
 - Psychotropic drugs.
- **Otological:**
 - Meniere's disease.
 - Labyrinthine ischemia.
 - Acoustic neuroma.



Diagnosis of the causes of falls

- A careful history should be taken.
- Physical examination including measurement of lying and standing blood pressures, full neurological, cardiac and joints examination.
- Investigations depends upon the clinical finding:
 - 1- 24 hour ECG.
 - 2- CT, MRI brain.
 - 3- Transcranial duplex.

Treatment

- Treatment of the cause.
- Programme of rehabilitation:
 - Physiotherapy.
 - Occupational therapy.
 - Speech therapy.
 - Care manager.

IV- Effects of aging on metabolism of drugs

There is high incidence of drug side effects, the risk can be minimized by starting off treatment with small doses and carefully monitoring the response. This is due to ↓ liver metabolism, ↓ renal excretion, ↓ lean body mass and ↑ body fat.

CLIMATE AND ENVIRONMENTAL FACTORS IN DISEASE

Heat disorders

I- Heat stroke (Heat hyperpyrexia)

It is due to overheating the body. It occurs when the core or rectal temperature rises through 41°C, it is associated with cessation of sweating and leads to tissue injury.

Risk factors

- Temperature $\geq 35^{\circ}\text{C}$.
- Humidity $\geq 75\%$.
- ↓ Sweating.
- Obesity.
- Dehydration.
- Febrile illness.

Clinical picture

- Loss of consciousness.
- Dry burning skin (hot dry man).
- It may be complicated by renal failure, LCF, DIC and shock.

Treatment

- Reduce body temp (remove clothes, body spray, with water).
- TTT of complication.



II- Hypothermia

It is defined as fall in the core temperature $< 35^{\circ}\text{C}$, it may be as low as 25°C . we can use thermocouple or low reading thermometer.

Causes

- Myxoedma.
- Alcohol abusers.
- Hypoglycemia.
- LCF.
- Addison's disease.
- Cold weather.

Clinical picture

- Tiredness.
- Stiff muscles.
- Heart rate and blood pressure fall.
- Ventricular fibrillation, coma.

Treatment: Warming – TTT of arrhythmia.

Lead poisoning

SOURCES

- Fuel additives released in automobile emissions.
- Lead water pipes and tanks.
- Lead soldered cans.
- Children may eat lead based paints.

C/P

- Fatigue, generalized body aches.
- Abdominal discomfort.
- Diarrhea.
- Peripheral neuropathy.
- Lead nephropathy.
- Blue lines on the gum.

Investigations: blood lead level.

Treatment

- Removal from exposure.
- Seizures treated by diazepam.
- Cerebral edema treated by Dexamethasone.
- Chelation by oral penicillamine.



METABOLIC DISEASES

1. Disorders of CHO metabolism

- Glycogen storage
 - DM
 - Hypoglycemia
- } See endocrine

2. Disorders of fat metabolism

Hyperlipidemia → see CVS

3. Disorders of protein metabolism

Generalized aminoaciduria (Fanconi \$).

Specific aminoaciduria (Cystinuria).

Alkaptonuria: due to homogentisic acid oxidase deficiency → homogentisic acid polymerizes to produce blue black product in cartilage and other tissue (Ochronosis) in nose and ear.

Homocystinuria: homocystin is excreted in urine with marfan like features and thrombotic episodes.

DISORDERS ASSOCIATED WITH DEFECTS IN ENZYMES (LYSOSOMAL STORAGE DISEASES)

1. Tay-Sachs disease:

Due to deficiency of hexosaminidase enzyme with accumulation of ganglioside → mental retardation, blindness (Accumulation of lipid in retina).

2. Neimann-Pick disease:

Due to deficiency of the sphingomyelinase with ↑ sphingomyelin
→ liver ++, spleen ++, neurological manifestations.

3. Gaucher's disease:

Due to deficiency of glucocerebrosidase with accumulation of glucocerebrosides → spleen ++, liver ++, and BM depression.

4. Mucopolysaccharidoses (MPS):

Deficiency of enzymes involved in the degradation of MPS → liver ++, spleen ++, narrowing of coronary, and mental retardation.

5. Glycogen storage diseases:

Defects in the synthesis or catabolism of glycogen e.g. Von Gierke's D due to deficiency of glucose -6- phosphatase → accumulation of glycogen with liver++ and hypoglycemia.



Amyloidosis

It is a group of diseases characterized by deposition of pathogenic fibrillar proteins that accumulate within tissues leading to organ and tissue dysfunction.

I- Systemic amyloidosis

1. B cell dyscrasias (1ry amyloidosis)

Composed of AL type amyloid i.e. immunoglobulins light chains derived from plasma cells, it can occur in MM. It affects heart, GIT, PN, skin, tongue, the light chains excreted in urine (Bence-Jones proteins).

2. 2ry amyloidosis or reactive amyloidosis:

Due to AA type amyloid associated with chronic inflammatory disorders. AA derived from serum precursors called SAA (Serum Amyloid Associated) protein synthesized in the liver. It affects kidney, liver, spleen, adrenals, and lymph nodes.

3. Hemodialysis related (Beta 2 microglobulin)

Beta 2 microglobulin not filtered by dialysis membrane.

4. Hereditary e.g. FMF → AA deposition.

II- Localized amyloidosis

e.g. Amyloidosis of age

- Senile cardiac amyloidosis (transthyretin).
- Senile cerebral amyloidosis (beta 2 amyloid protein) found in Alzheimer's disease.

C/P of amyloidosis

- Kidney → nephrotic \$, renal tubular acidosis and chronic renal failure.
- Heart → cardiomyopathy.
- PN → neuropathy & carpal tunnel \$.
- Arthropathy.
- Liver ++, spleen ++, macroglossia.
- CNS involvement.

Diagnosis

Biopsy showing red colour with cong-red and gives a yellow green fluorescence in polarized light. Favored biopsy sites are rectum, gingiva in systemic disease and from kidney when renal manifestations are present.

Treatment

- TTT of the cause.
- Symptomatic.
- Colchicines for TTT of FMF.
- Chemotherapy may be effective in AL type!?

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- 1- Hepatology.
- 2- Gastroenterology.
- 3- Endocrinology.
- 4- Rheumatology.
- 5- Cardiology.
- 6- Nephrology.
- 7- Hematology.
- 8- Neurology and psychiatry.
- 9- Infectious diseases, tropical diseases, immunology, nutrition, genetics, geriatric, toxicology and therapeutics.
- 10- Respiratory diseases.
- 11- Clinical medicine (symptoms and examination).
 - Cardiology.
 - Chest.
 - Abdomen.
 - Neurology.
 - General.

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